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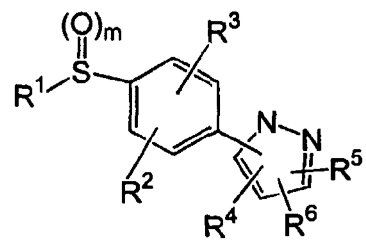
(54) Title: PYRAZOLES HAVING ANTIINFLAMMATORY ACTIVITY

(57) Abstract

The present invention relates to novel antiinflammatory compounds, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their regioisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them. More particularly, the present invention relates to novel heterocyclic compounds of general the formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their regioisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them.

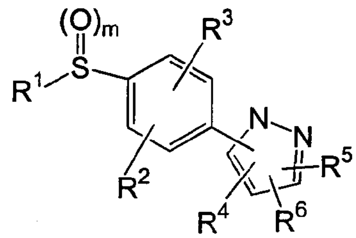


(I)

PYRAZOLES HAVING ANTIINFLAMMATORY ACTIVITY

Field of the Invention

The present invention relates to novel antiinflammatory compounds, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their regioisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them. More particularly, the present invention relates to novel heterocyclic compounds of the general formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their regioisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them.



(I)

The present invention also relates to a process for the preparation of the above said novel compounds, their analogs, their derivatives, their tautomeric forms, their stereoisomers, their regioisomers, their polymorphs, their pharmaceutically acceptable salts, pharmaceutically acceptable solvates and pharmaceutical compositions containing them.

The present invention also relates to novel intermediates, process for their preparation and their use in the preparation of compounds of formula (I).

The compounds of general formula (I) are useful as antiinflammatory, analgesic, antipyretic, antiarthritic, antibacterial, anticancer agents or for treating Alzheimer diseases. The compounds of the present invention are also useful for the treatment of

diseases of human or animals such as pain, fever or inflammation. Compounds of formula (I) also inhibit prostanoid-induced smooth muscle contraction by preventing the synthesis of contractile prostanoids and hence may be of use in the treatment of dysmenorrhea, premature labor and asthma. The compounds of the present invention are useful for treatment of pain, fever, and inflammation related to common cold, influenza, viral infections. The compounds of the present invention can be used for the treatment of arthritis such as rheumatoid arthritis, osteoarthritis, gouty arthritis, juvenile arthritis, spondylo arthritis; systemic lupus erythematosus, skin inflammation disorders such as eczema, burns, dermatitis, psoriasis; low back and neck pain, head ache, tooth ache, sprains, strains, myostis, neuralgia, synovitis, bursitis, tendinitis, injuries following surgical and dental procedures, post-operative inflammation including ophthalmic surgery such as cataract and refractive surgery.

The compounds of general formula (I) are also useful for the treatment of dysmenorrhoea, premature labour, asthma and bronchitis, gastrointestinal conditions such as inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, ulcerative colitis, diverticulitis, regional enteritis, peptic ulcers. These compounds may also be useful for treating inflammation in diseases such as vascular diseases, migraine head aches, periarteritis nodosa, thyroiditis, aplastic anemia, Behcat's syndrome, Hodgkin's diseases, scleroderma, myasthenia gravies, sarcoidosis, nephrotic syndrome, Type I diabetes, polymyositis, conjunctivitis, gingivitis, myocardial ischaemia, nephritis, swelling after injury, hypersensitivity and the like. The compounds of the present inventions are useful in the treatment of allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, and central nervous system damage resulting from stroke, ischaemia and trauma; pulmonary inflammation such as in the case of viral infections and cystic fibrosis; ophthalmic diseases such as retinitis, retinopathy, uveitis, ocular photophobia and acute injury to eye tissues. The compounds of general formula (I) are also useful for treating central nervous system disorders such as cortical dementia (Alzheimer's diseases), useful for treatment of pain not limited to dental pain, muscular pain, pain from cancer, postoperative pain, and

useful for the treatment of diseases where NSAIDS are used with the benefit of having significantly less side effects.

The compounds of general formula (I) are cyclooxygenase inhibitors and are therefore useful to treat the cyclooxygenase mediated diseases. The compounds of formula (I) are also useful for the treatment of mammals not limited to human beings such as horses, dogs, cats, sheep, pigs etc., and also for treating rats, mice, rabbits etc. The compounds of formula (I) may also be used in cotherapies for inflammation, Alzheimer's disease or cancer, in place of, or together with the conventional therapies.

The compounds of the general formula (I) are useful as partial or complete substitute for NSAIDS in compositions or preparations wherein they are presently coadministered with other agents or ingredients. The present invention also comprises pharmaceutical compositions for treating cyclooxygenase mediated diseases as defined earlier, comprising a non-toxic therapeutically effective amount of the compound of formula (I) as defined above and pharmaceutically acceptable carrier optionally containing one or more ingredients such as another analgesic agent like acetaminophen of phenacetin, a potentiator like caffeine, a H_2 antagonist, aluminum or magnesium hydroxide, simethicone, a decongestant such as phenylephrine, phenyl propanolamine, pseudophedrine, oxymetazoline, epinephrine, nephazoline, propylhexadrine or leavo-desoxyephedrine, xylomatezoline, a sedating or non sedating antihistamine, an antitussive such as dextromethorphan, carbetapentane, caramiphen, hydrocodeine and codeine and the like, or a diuretic agent. The present invention also comprises a method of treatment of cyclooxygenase mediated diseases consisting of administering a patient in need thereof, a nontoxic therapeutically effective amount of compound of formula (I) or pharmaceutical composition described above.

Background of Invention

Nonsteroidal anti-inflammatory drugs (NSAIDS) are widely used in the treatments of arthritis and pain. These agents act by inhibiting the production of prostaglandin, which plays an important role in the inflammation process. The

prostaglandin synthesis is inhibited by blocking the enzyme cyclooxygenase (COX) (Vane J. R. Nature [New Biol.] 1971, 231-232). However, these NSAIDS while reducing the prostaglandin induced inflammation and associated symptoms, have also been found to affect prostaglandin regulated other beneficial processes causing side effects [Allison M. C, et.al., J. Med. 1992, 327, 749]. The side effects showed by NSAIDS are gastrointestinal ulceration and intolerance, blockade of platelet aggregation, inhibition of uterine motility, inhibition of prostaglandin mediated renal function and hypersensitivity reactions.

Recently, it has been discovered that two isoforms of cyclooxygenase enzyme exist viz., COX-1 and COX-2. While COX-1 is constitutive isoform found in blood vessels, stomach and kidney, COX-2 is induced during inflammation. Therefore, selective inhibition of COX-2 enzyme would be useful in treating inflammation without causing side effects due to inhibition of COX-1.

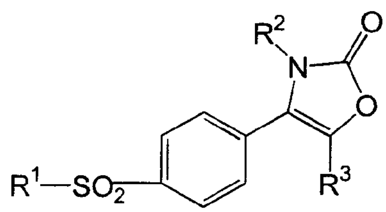
Alternatively Leukotriens also are mediators of inflammation and related disorders. The leukotriens (LTB4, LTC4, LTD4 etc.,) are produced by the 5-lipoxygenase mediated oxidation of arachidonic acid. Hence inhibition of 5-lipoxygenase (5-LO) enzyme would also be useful in treating inflammation and related disorders. It is therefore possible to treat inflammation with agents which can selectively inhibit COX-2 or 5-LO or both without causing the potential side effects caused by chronic treatment with common NSAIDS.

Recently it has been shown that there is increased expression of COX-2 in colon tumors. Therefore, agents that can inhibit COX-2 can also be used in the treatment of cancer.

Studies have shown that the brain tissues of patients of Alzheimer's disease often have high levels of COX-2. This indicates the usefulness of COX-2 inhibitors in the treatment of Alzheimer's disease and in enhancing the memory.

A few heterocyclic compounds, their derivatives, and their analogs have been reported to be useful in the treatment of inflammation. Some of such compounds described in the prior art are outlined below:

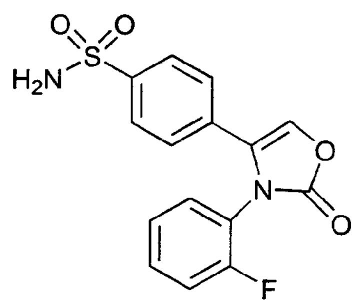
(i) International patent application No. WO 97/34882 discloses compounds of general formula (IIa)



(IIa)

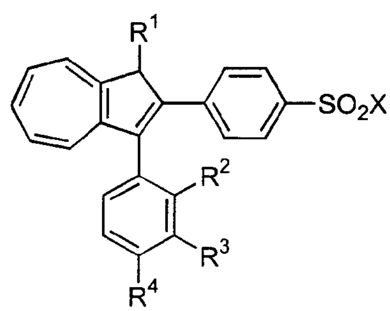
wherein R^1 is an alkyl or NR^4R^5 group, wherein R^4 and R^5 each independently is hydrogen or an alkyl or benzyl group; R^2 is a naphthyl, tetrahydronaphthyl, unsubstituted phenyl or phenyl group, substituted by from 1 to 3 halogen atoms, alkyl, hydroxy, alkoxy or trifluoromethyl groups and R^3 is hydrogen or an alkyl group.

An example of these compounds is shown in formula (IIb)



(IIb)

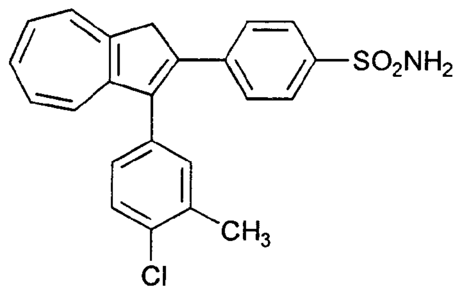
(ii) DE patent No. 19753463 discloses compounds of formula (IIc)



(IIc)

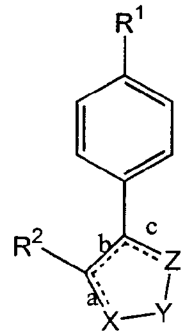
wherein R^1 represents hydrogen, alkoxycarbonyl, carboxy, halo, alkyl, phenyl or alkanoyl; R^2, R^3 and R^4 represents hydrogen, alkyl, alkoxy or halo; X represents alkyl or NH_2.

An example of these compounds is shown in formula (IId)



(IId)

(iii) International patent application No. WO 95/00501 discloses compounds of formula (IIe)

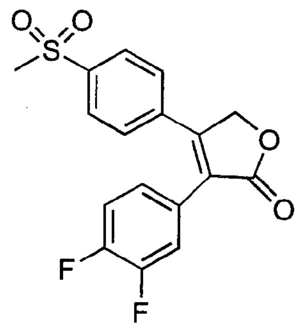


(IIe)

wherein X-Y-Z- is selected from the group consisting of $-CH_2CH_2CH_2-$, $-C(O)CH_2CH_2-$, $-CH_2CH_2C(O)-$, $CR^5(R^{5'})-O-C(O)-$, $-C(O)-O-CR^5(R^{5'})-$, $CH_2-NR^3-CH_2-$, $CR^5(R^{5'})-NR^3-C(O)-$, $-CR^4=CR^{4'}-S-$, $-S-CR^4=CR^{4'}-$, -S-N=CH-, -CH=N-S-, $-N=CR^4-O-$, $-O-CR^4=N-$, $-N=CR^4-NH-$, $-N=CR^4-S-$, $-S-CR^4=N-$, $-C(O)-NR^3-CR^5(R^{5'})-$, $-NR^3-CH=CH-$ provided R^1 is other than $-S(O)_2Me$, $-CH=CH-NR^3-$ provided R^1 is other than $-S(O)_2Me$; when side b is a double bond and sides a and c are single bonds and X-Y-Z- is selected from the group consisting of =CH-O-CH=, $=CH-NR^3-CH=$, =N-S-CH=, =CH-S-N=, =N-O-CH=, =CH-O-N=, =N-S-N=, =N-O-N=, when sides a and c are double bonds and side b is a single bond; R^1 is selected from the group consisting of $S(O)_2CH_3$, $S(O)_2NH_2$, $S(O)_2NHC(O)CF_3$, $S(O)(NH)CH_3$, $S(O)(NH)NH_2$, $S(O)(NH)NHC(O)CF_3$, $P(O)(CH_3)OH$ and $P(O)(CH_3)NH_2$; R^2 is selected from the group consisting of (C_1-

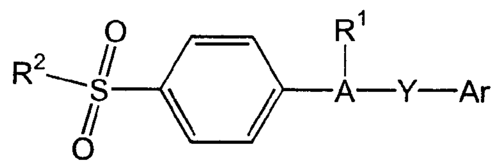
C_6)alkyl; (C_3-C_7)cycloalkyl; mono, di or tri substituted phenyl wherein the substituent is selected from the group consisting of hydrogen, halo, (C_1-C_6)alkoxy, (C_1-C_6)alkylthio, CN, CF_3, (C_1-C_6)alkyl, N_3, -CO_2H, -CO_2-(C_1-C_4)alkyl, -C(R^5)(R^6)-OH, -C(R^5)(R^6)-O-(C_1-C_4)alkyl and –(C_1-C_6)alkyl-CO_2-R^5; mono, di or tri substituted heteroaryl wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one hetero atom which is S, O or N and optionally 1, 2, 3 or 4 additional N atoms, said substituents are selected from the group consisting of hydrogen, halo including fluoro, chloro, bromo and iodo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkylthio, CN, CF_3, N_3, -C(R^5)(R^6)-OH and , -C(R^5)(R^6)-O-(C_1-C_4)alkyl; R^3 is selected from the group consisting of hydrogen, CF_3, CN, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, -C(O)-(C_1-C_6)alkyl and optionally substituted -(C_1-C_5)alkyl-Q, -(C_1-C_3)alkyl-O-(C_1-C_3)alkyl-Q, -(C_1-C_3)alkyl-S-(C_1-C_3)alkyl-Q, -(C_1-C_5)alkyl-O-Q, or -(C_1-C_5)alkyl-S-Q, wherein the substituents resides on the alkyl and the substituent is (C_1-C_3)alkyl; or R^3 represents –Q; R^4 and $R^{4'}$ are each and independently selected from the group consisting of hydrogen, CF_3, CN, (C_1-C_6)alkyl, -Q, -O-Q, -S-Q, and optionally substituted (C_1-C_5)alkyl-Q, -O-(C_1-C_5)alkyl-Q , -S-(C_1-C_5)alkyl-Q, -(C_1-C_3)alkyl-O-(C_1-C_3)alkyl-Q, -(C_1-C_3)alkyl-S-(C_1-C_3)alkyl-Q, -(C_1-C_5)alkyl-O-Q, or -(C_1-C_5)alkyl-S-Q, wherein the substituents resides on the alkyl and the substituent is (C_1-C_3)alkyl; and R^5, $R^{5'}$, R^6, R^7 and R^8 are each independently selected from the group consisting of hydrogen, (C_1-C_6)alkyl or R^5, $R^{5'}$, R^6, R^7 and R^8 together with the carbon to which they are attached form a monocyclic saturated carbon ring of 3, 4, 5, 6, or 7 atoms. Q is CO_2H, CO_2-(C_1-C_4)alkyl, tetrazolyl-5-yl, C(R^7)(R^8)(OH), or C(R^7)(R^8)(O-(C_1-C_4)alkyl; provided that when X-Y-Z is S-CR^4=C$R^{4'}$, then R^4 and $R^{4'}$ are other than CF_3.

An example of these compounds is shown in formula (IIf)



(IIf)

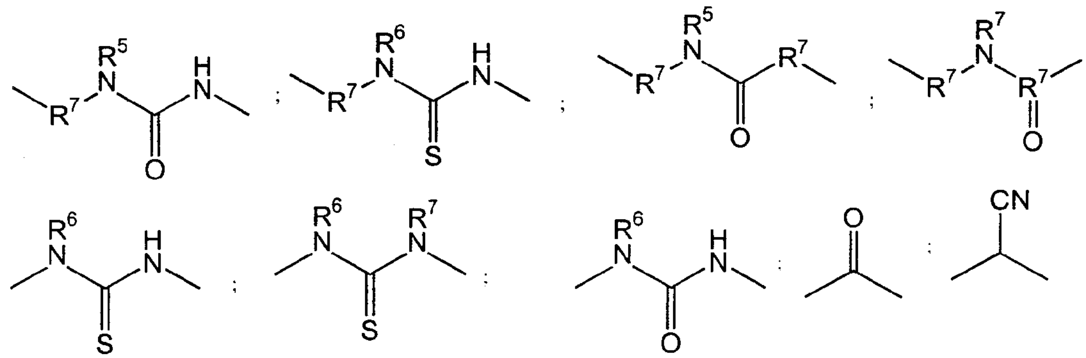
(iv) International patent application No. WO 96/38442 discloses compounds of formula (IIg)



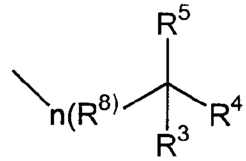
(IIg)

wherein A is a 5 or 6 membered ring substituent selected from partially unsaturated or unsaturated heterocycle and carbocyclic rings, A may be optionally substituted with a radical selected from acyl, halo, alkyl, haloalkyl, cyano, nitro, carboxyl, alkoxy, oxo, aminocarbonyl, alkoxycarbonyl, carboxyalkyl, cyanoalkyl and hydroxyalkyl; Y is a radical selected from oxy, thio, sulfinyl, sulfonyl, alkyl, alkenyl, alkynyl, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, hydroxyalkyl, hydroxyalkyloxy, hydroxyalkyloxyalkyl, hydroxyalkylthio, hydroxyalkylthioalkyl, oximinoalkoxy, oximinoalkoxyalkyl, (alkyl)oximinoalkoxy, (alkyl)oximinoalkoxyalkyl, oximinoalkylthio, oximinoalkylthioalkyl, (alkyl)oximinoalkylthio, (alkyl)oximinoalkylthioalkyl, carbonylalkyloxy, carbonylalkyloxyalkyl, carbonylalkylthio, carbonylalkylthioalkyl, heterocyclyl, cycloalkenyl, aralkyl, heterocycloalkyl, acyl, alkylthioalkyl, alkyloxyalkyl, alkenylthio, alkynylthio, alkenyloxy, alkynyloxy, alkenylthioalkyl, alkenyloxyalkyl, alkynyloxyalkyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkylarylalkynyloxy, alkylarylalkenyloxy, alkylarylalkynylthio, alkylarylalkenylthio, haloalkylcarbonyl, alkoxyalkyl, alkylaminocarbonylalkyl, heteroaralkoxyalkyl, heteroaryloxyalkyl, heteroarylthioalkyl, heteroaralkylthioalkyl, heteroaralkoxy, heteroaralkylthio, heteroaryloxy, heteroarylthio,

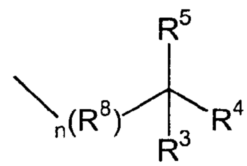
arylthioalkyl, aryloxyalkyl, haloaryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, alkoxycarbonylcyanoalkenyl, aminocarbonylalkyl, N-alkylaminocarbonyl, N-arylaminocarbonyl, N,N-dialkylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, cycloalkylaminocarbonyl, heterocycloaminocarbonyl, carboxyalkylaminocarbonyl, alkylcarbonylalkyl, aralkoxycarbonylalkylaminocarbonyl, haloaralkyl, carboxyhaloalkyl, alkoxycarbonylhaloalkyl, aminocarbonylhaloalkyl, alkylaminocarbonylhaloalkyl, N-alkylamino, N,N-dialkylamino, N-arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-arylamino, aminoalkyl, N-alkylaminoalkyl, N,N-dialkylaminoalkyl, N-arylaminoalkyl, N-aralkylaminoalkyl, N-alkyl-N-aralkylaminoalkyl;. N-alkyl-N-arylaminoalkyl, aminoalkoxy, aminoalkoxyalkyl, aminoalkylthio, aminoalkylthioalkyl, cycloalkyloxy, cycloalkylalkyloxy, cycloalkylthio, cycloalkylalkylthio, aryloxy, aralkoxy, arylthio, aralkylthio, aralkylsulfinyl, alkylsulfonyl aminosulfonyl, N-alkylaminosulfonyl, N-arylaminosulfonyl, arylsulfonyl, N,N-dialkylaminosulfonyl, N-alkyl-N-arylaminosulfonyl, or Y represents following groups



Ar is selected from aryl and heteroaryl, Ar may be optionally substituted with one or two substituents selected from halo, hydroxyl, mercapto, amino, nitro, cyano, carbamoyl, alkyl, alkenyloxy, alkoxy, alkylthio, alkylsulfonyl, alkylsulfinyl, alkylamino, dialkylamino, haloalkyl, alkoxycarbonyl, N-alkylcarbamoyl, N,N-dialkylcarbamoyl, alkanoylamino, cyanoalkoxy, carbamoylalkoxy, alkoxycarbonylalkoxy, and

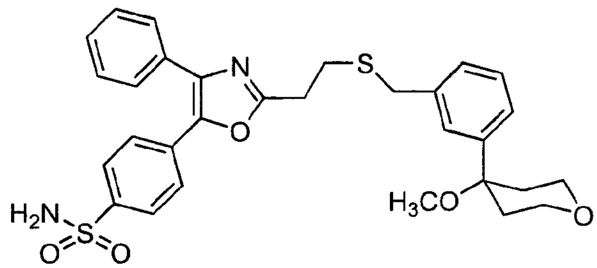


where R^1 is one or more substituents selected from heterocycle, cycloalkyl, cycloalkenyl, and aryl, R^1 may be optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio; R^2 is selected from alkyl and amino; wherein R^3 and R^4 together form a group of the formula -B-X-B^1 which together with the carbon atom to which B and B^1 are attached defines a ring having 6 ring atoms, wherein B and B^1 which may be the same or different, each is alkylene and X is oxy, and which ring may bear one, two or three substituents, which may be the same or different selected from hydroxyl, alkyl, alkoxy, alkenyloxy and alkynyloxy; wherein R^5 is selected from hydroxyl, alkoxy, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyl, acyl, and cyano; wherein R^6 is selected from hydrido, alkyl, aryl, and aralkyl; wherein R^7 is selected from alkyl, alkoxy, alkenyl, and alkynyl; wherein R^8 is oximino optionally substituted with alkyl; wherein n is 0 or 1; provided Ar is substituted with

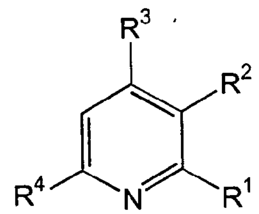


where R^3, R^4 R^5, R^8 and n are as defined above

An example of these compounds is shown in formula (IIh)


(IIh)

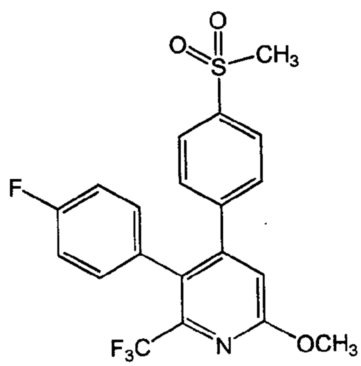
(v) International application WO 96/24585 discloses compounds of formula (IIi)



(IIi)

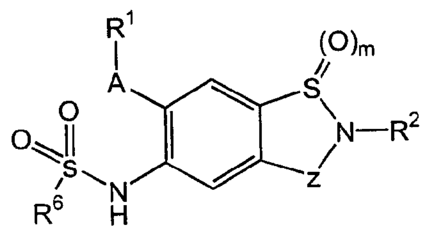
wherein R^1 is haloalkyl; R^2 is aryl optionally substituted at a substitutable position with one or more radicals independently selected from alkylsulfinyl, alkyl, cyano, carboxyl, alkoxycarbonyl, haloalkyl, hydroxyl, hydroxyalkyl, haloalkyl, amino, alkylamino, arylamino, nitro, halo, alkoxy and alkylthio; R^3 is aryl substituted at a substitutable position with a radical selected from alkylsulfonyl and sulfamyl and R^4 is selected from halo, alkoxy, and alkynyloxy.

An example of these compounds is shown in formula (IIj)



(IIj)

(vi) German patent DE 19533643 discloses compounds of formula (IIk)

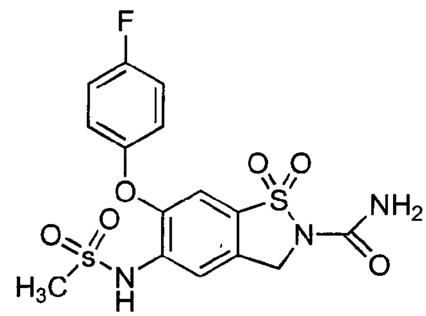


(IIk)

wherein A is O, S or NH; R^1 is optionally substituted cycloalkyl, aryl or heteroaryl; R^2 is hydrogen, optionally substituted alkyl, aralkyl, aryl, heteroaryl, or $(CH_2)_n$-X; Z is CH_2, CH_2CH_2, $CH_2CH_2CH_2$, $CH_2CH=CH$, CH_2CO, NHCO, $NHCH_2$, N=CH, NHCH, CH_2CH_2NH, CH=CH, C=O, $S(O)_m$ or optionally substituted NH; m is 0-2; n is 0-8; X is halo, NO_2, optionally substituted OH, COH, COOH, OCOOH, CONHOH, $CONH_2$, SH,

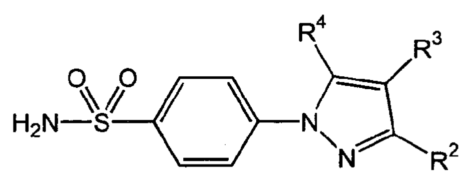
S(O)H, SO_2H, NH_2, NHCOH or $NHSO_2H$ or CN; R^6 is optionally substituted (C_1-C_4)alkyl.

An example of these compounds is shown in formula (III)



(III)

(vii) International patent application WO 95/15316 discloses compounds of formula (IIm)

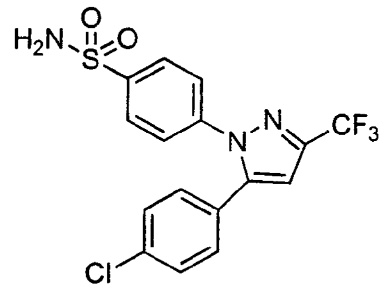


(IIm)

wherein R^2 is selected from hydrido, alkyl, haloalkyl, alkoxycarbonyl, cyano, cyanoalkyl, carboxy, aminocarbonyl, alkylaminocarbonyl, cycloalkylaminocarbonyl, arylaminocarbonyl, carboxyalkylaminocarbonyl, carboxyalkyl, aralkoxycarbonylalkylaminocarbonyl, aminocarbonylalkyl, alkoxycarbonyl, cyanoalkenyl and hydroxyalkyl; wherein R^3 is selected from hydrido, alkyl, cyano, hydroxyalkyl, cycloalkyl, alkylsulfonyl, and halo; R^4 is selected from aralkenyl, aryl, cycloalkyl, cycloalkenyl and heterocyclic, R^4 is optionally substituted at a substitutable position with one or more radicals selected from halo, alkylthio, alkylsulfonyl, cyano, nitro, haloalkyl, alkyl, hydroxyl, alkenyl, hydroxyalkyl, carboxyl, cycloalkyl, alkylamino, dialkylamino, alkoxycarbonyl, aminocarbonyl, alkoxy, haloalkoxy, sulfamyl, heterocyclic and amino; provided R^2 and R^3 are not both hydrido; further provided that R^2 is not carboxyl, or methyl when R^3 is hydrido and when R^4 is phenyl; further provided that R^4 is not triazolyl when R^2 is methyl; further provided that R^4 is not aralkenyl when R^2 is carboxyl, aminocarbonyl or ethoxycarbonyl; further provided

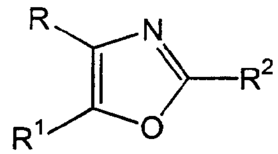
that R^4 is not phenyl when R^2 is methyl and R^3 is carboxyl; and further provided that R^4 is not unsubstituted thienyl when R^2 is trifluoromethyl.

An example of these compounds is shown in formula (IIn)



(IIn)

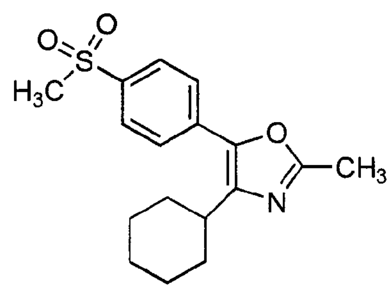
(viii) International patent application WO 96/19462 discloses compounds of formula (IIo)



(IIo)

wherein one of R, R^1 is methylsulfonylphenyl, aminosulfonylphenyl or alkylaminosulfonylphenyl and the other is 5-7carbon cycloalkyl optionally substituted by alkyl, thienyl or furyl optionally substituted by alkyl or halo; R^2 is lower alkyl.

An example of these compounds is shown in formula (IIp)



(IIp)

Summary of the Invention

With an objective to develop novel compounds for the treatment and / or prophylaxis of diseases of cyclooxygenase, more particularly COX-2 and other related diseases such as pain, fever or inflammation, to inhibit prostanoid-induced smooth muscle contraction, to treat Alzheimer disease, colorectal cancer, for the treatment of pain, fever, and

inflammation related to common cold, influenza, viral infections, for the treatment of arthritis such as rheumatoid arthritis, osteoarthritis, gouty arthritis, juvenile arthritis, spondylo arthritis; systemic lupus erythematosus, skin inflammation disorders such as eczema, burns, dermatitis, psoriasis; low back and neck pain, dysmenorrhoea, head ache, tooth ache, sprains, strains, myostis, neuralgia, synovitis, bursitis, tendinitis, injuries following surgical and dental procedures, post-operative inflammation including ophthalmic surgery such as cataract and refractive surgery, with better efficacy, potency and lower toxicity, we focussed our research to develop new compounds effective in the treatment of above mentioned diseases. Effort in this direction has led to the development of compounds having general formula (I).

The main objective of the present invention is therefore, to provide novel compounds and their derivatives, their analogs, their tautomeric forms, their stereoisomers, their regioisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutical compositions containing them, or their mixtures.

Another objective of the present invention is to provide novel compounds and their derivatives, their analogs, their tautomeric forms, their stereoisomers, their regioisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutical compositions containing them or their mixtures having enhanced activities, without toxic effect or with reduced toxic effect.

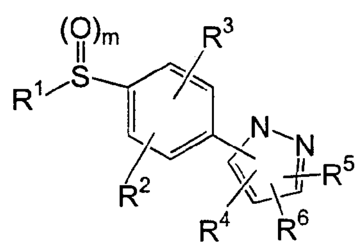
Yet another objective of the present invention is to produce a process for the preparation of novel compounds and their derivatives of the formula (I) as defined above, their analogs, their tautomeric forms, their stereoisomers, their regioisomers, their polymorphs, their pharmaceutically acceptable salts and their pharmaceutically acceptable solvates.

Still another objective of the present invention is to provide pharmaceutical compositions containing compounds of the general formula (I), their analogs, their derivatives, their tautomers, their stereoisomers, their regioisomers, their polymorphs, their salts, solvates or their mixtures in combination with pharmaceutically acceptable carriers, solvents, diluents and other media normally employed in preparing such compositions, optionally containing one or more ingredients such as another analgesic agent like acetaminophen of phenacetin, a potentiator like caffeine, a H_2 antagonist, aluminum or magnesium hydroxide, simethicone, a decongestant such as phenylephrine, phenyl propanolamine, pseudophedrine, oxymetazoline, epinephrine, nephazoline, propylhexadrine or leavo-desoxyephedrine, xylomatazoline, a sedating or non sedating antihistamine, an antitussive such as dextromethorphan, carbetapentane, caramiphen, hydrocodeine and codeine and the like, or a diuretic agent.

The present invention also provides a method for the treatment of cyclooxygenase mediated diseases consisting of administering a patient in need thereof, a nontoxic therapeutically effective amount of compound of formula (I) or pharmaceutical composition described above.

Detailed Description of the Invention

The present invention relates to compounds having the general formula (I)



(I)

wherein R^1 represents amino or substituted or unsubstituted groups selected from alkyl, alkylamino, acylamino, cycloalkyl, cyclicamino, carboethoxycarbonylalkyl, hydrazino, hydrazido, aminoacid residue, aryl, heteroaryl or $-N=CR(NR)_2$ where R represents hydrogen or lower alkyl group; R^2 represents cyano, nitro, azido, formyl, oximealkyl, thio or substituted or unsubstituted groups selected from amino, alkoxy,

hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacid residuealkyl, acyl, carbonyloxyalkyl, haloalkyl, aminoalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, thioalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, aralkoxyalkyl, carbonylalkyl, carboxamidoalkyl or carbonylaminoalkyl groups; R^3 represents hydrogen, halogen atom, hydroxy, nitro, cyano, azido or substituted or unsubstituted groups selected from hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, alkyl, alkoxy, hydroxyalkyl, alkoxyalkyl, acylamino or amino groups; R^4, R^5 and R^6 when attached to carbon atom may be same or different and independently represent hydrogen, halogen, hydroxy, cyano, nitro, thio, oxo, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, aralkoxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, aromatic, single or fused, carbocycle or heterocycle ring; R^4, R^5 and R^6 when attached to nitrogen atom may be same or different and represent hydrogen, hydroxy, cyano, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, single or fused, aromatic, carbocycle or heterocycle groups; the pyrazole ring may be fused with R^4, R^5 or R^6 wherever possible and m is an integer in the range of 0-2.

Suitable groups represented by R^1 may be selected from amino, hydrazino, which may be substituted; hydrazido, which may be substituted; aminoacid residue, wherein the aminoacid is selected from glycine, alanine, phenylalanine, lysine and the like, which may be substituted; substituted or unsubstituted linear or branched (C_1-C_6)alkyl group such as methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, t-butyl, n-pentyl, isopentyl, hexyl and the like; alkylamino group such as methylamino, ethylamino, propylamino, butylamino, pentylamino, hexylamino and the like, which may be substituted; acylamino groups such as $NHCOCH_3$, $NHCOC_2H_5$, $NHCOC_3H_7$, $NHCOC_6H_5$ and the like, which may be substituted; cycloalkyl group such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and the like, which may be substituted; cyclic amino group such as aziridine, pyrrolidine, piperidine, and the like, the cyclic amino group may be substituted; carboethoxycarbonylalkyl group such as carboethoxycarbonylmethyl, carboethoxycarbonylethyl, carboethoxycarbonylpropyl and the like, which may be substituted; aryl group such as phenyl, naphthyl and the like, the aryl group may be substituted; heteroaryl group such as pyrrole, furan, pyridine, thiophene and the like, the heteroaryl group may be substituted. The substituents may be selected from halogen atom such as chlorine, fluorine, bromine or iodine; hydroxy, nitro, amino, cyano, alkyl, alkoxy, acyl, aryl, aralkyl or heteroaryl groups.

Suitable groups represented by R^2 may be selected formyl, cyano, nitro, azido, thio, oximealkyl groups such as oximemethyl, oximeethyl, oximepropyl and the like; halo(C_1-C_6)alkyl, which may be substituted; (C_1-C_6)alkoxy such as methoxy, ethoxy, propyloxy, butyloxy, iso-propyloxy and the like, which may be substituted; halo(C_1-C_6)alkoxy, which may be substituted; hydroxy(C_1-C_6)alkyl, which may be substituted; alkoxyalkyl group such as methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl and the like, which may be substituted; amino(C_1-C_6)alkyl, which may be substituted; thio(C_1-C_6)alkyl, which may be substituted; hydrazino, which may be substituted; hydrazinoalkyl group such as hydrazinomethyl, hydrazinoethyl, hydrazinopropyl and the like, which may be substituted; hydrazido, which may be substituted; hydrazidoalkyl such as hydrazidomethyl, hydrazidoethyl, hydrazidopropyl and the like, which may be

substituted; aminoacid residue, wherein the aminoacid is selected from glycine, alanine, phenylalanine, lysine and the like, which may be substituted; aminoacid residue (C_1-C_6)alkyl wherein the aminoacid is as defined above, which may be substituted; acyl group such as acetyl, propanoyl, benzoyl and the like, which may be substituted; aryl group such as phenyl, naphthyl and the like, the aryl group may be substituted; aralkyl such as benzyl, phenethyl, $C_6H_5CH_2CH_2CH_2$, naphthylmethyl and the like, the aralkyl group may be substituted; aryloxy group such as phenoxy, naphthyloxy and the like, the aryloxy group may be substituted; aralkoxy group such as benzyloxy, phenethyloxy, naphthylmethyloxy, phenylpropyloxy and the like, which may be substituted; aryloxyalkyl group such as $C_6H_5OCH_2$, $C_6H_5OCH_2CH_2$, naphthyloxymethyl and the like, which may be substituted; aralkoxyalkyl group such as $C_6H_5CH_2OCH_2$, $C_6H_5CH_2OCH_2CH_2$ and the like, which may be substituted; linear or branched (C_1-C_6)alkylthio, which may be substituted; (C_1-C_6)alkylsulfinyl such as methylsulfinyl, ethylsulfinyl, propylsulfinyl, and the like, which may be substituted; (C_1-C_6)alkylsulfonyl group such as methylsulfonyl, ethylsulfonyl, propylsulfonyl and the like, which may be substituted; amino group, which may be substituted; carbonyloxyalkyl group such as carbonyloxymethyl, carbonyloxyethyl, carbonyloxypropyl and the like, which may be substituted; carbonylalkyl group such as carbonylmethyl, carbonylethyl, carbonylpropyl and the like, which may be substituted; carboxamidoalkyl; carbonylaminoalkyl group such as carbonylaminomethyl carbonylaminoethyl, carbonylaminopropyl and the like, which may be substituted. The substituents may be selected from halogen atom such as chlorine, fluorine, bromine or iodine; hydroxy, nitro, amino, thio, cyano, alkyl, haloalkyl, haloalkoxy, acyl, acyloxy, aryl, alkoxy, aralkyl, aralkoxy or carboxy groups.

Suitable groups represented by R^3 may be selected from hydrogen, halogen atom such as chlorine, fluorine, bromine or iodine; hydroxy, nitro, cyano, azido, hydrazino, which may be substituted; hydrazinoalkyl groups such as hydrazinomethyl, hydrazinoethyl, hydrazinopropyl and the like, which may be substituted; hydrazido, which may be substituted; hydrazidoalkyl such as hydrazidomethyl, hydrazidoethyl,

hydrazidopropyl and the like, which may be substituted; aminoacid residue, wherein the aminoacid is selected from glycine, alanine, phenylalanine, lysine and the like, which may be substituted; linear or branched $(C_1\text{-}C_6)$alkyl group such as methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, t-butyl, n-pentyl, isopentyl, hexyl and the like, which may be substituted; $(C_1\text{-}C_6)$alkoxy such as methoxy, ethoxy, propyloxy, butyloxy, iso-propyloxy and the like, which may be substituted; hydroxy$(C_1\text{-}C_6)$alkyl, which may be substituted; amino group, which may be substituted; acylamino groups such as $NHCOCH_3$, $NHCOC_2H_5$, $NHCOC_3H_7$, $NHCOC_6H_5$ and the like; $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl group such as methoxymethyl, ethoxymethyl, methoxyethyl, ethoxypropyl and the like. The substituents may be selected from nitro, halogen, amino, thio or cyano groups.

Suitable groups represented by R^4, R^5 and R^6 are selected from hydrogen, halogen atom such as fluorine, chlorine, bromine, or iodine; hydroxy, cyano, nitro, thio, oxo, hydroxylamino, substituted or unsubstituted linear or branched $(C_1\text{-}C_6)$alkyl group such as methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, t-butyl, n-pentyl, isopentyl, hexyl and the like; $(C_1\text{-}C_6)$alkoxy such as methoxy, ethoxy, propoxy, butoxy and the like, the alkoxy groups may be substituted; acyl group such as formyl, acetyl, propanoyl, benzoyl and the like; the acyl group may be substituted; acyloxy group such as OCOMe, OCOEt, OCOPh and the like, the acyloxy group may be substituted; amino group, which may be substituted; hydrazino, which may be substituted; hydrazinoalkyl groups such as hydrazinomethyl, hydrazinoethyl, hydrazinopropyl and the like, which may be substituted; hydrazido, which may be substituted; hydrazidoalkyl such as hydrazidomethyl, hydrazidoethyl, hydrazidopropyl and the like, which may be substituted; aminoacid residue, wherein the aminoacid is selected from glycine, alanine, phenylalanine, lysine and the like, which may be substituted; aminoacyl such as aminoacetyl, aminopropanoyl, aminobutanoyl and the like, which may be substituted; aryl group such as phenyl, naphthyl and the like, the aryl group may be substituted; aralkyl such as benzyl, phenethyl, $C_6H_5CH_2CH_2CH_2$, naphthylmethyl and the like, the aralkyl group may be substituted; aryloxy group such as phenoxy, naphthyloxy and the

like, the aryloxy group may be substituted; aralkoxy group such as benzyloxy, phenethyloxy, naphthylmethyloxy, phenylpropyloxy and the like, which may be substituted; carboxyalkyl such as carbomethoxy, carboethoxy, carbopropoxy and the like, which may be substituted; carboxyalkenyl such as carboxyethenyl, carboxypropenyl, carboxybutenyl and the like, which may be substituted; (C_1-C_6)alkoxycarbonyl such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl and the like, which may be substituted; aryloxycarbonyl such as phenoxycarbonyl, naphthyloxycarbonyl and the like, which may be substituted; aralkoxycarbonyl group such as benzyloxycarbonyl, phenethyloxycarbonyl, naphthylmethoxycarbonyl and the like, which may be substituted; carbonylamino, which may be substituted; aminocarbonylalkyl such as aminocarbonylmethyl, aminocarbonylethyl, aminocarbonylpropyl and the like, which may be substituted; alkylaminoalkoxy groups such as methylaminomethoxy, ethylaminoethoxy, methylaminoethoxy, ethylaminomethoxy, propylaminoethoxy and the like, the alkylaminoalkoxy group may be substituted; alkylaminoacyl groups such as methylaminoacetyl, ethylaminopropanoyl, methylaminopropanoyl, ethylaminoacetyl and the like, the alkylaminoacyl group may be substituted; cycloalkylacylamino, which may be substituted; substituted or unsubstituted carbocyclic groups such as phenyl, indenyl, dihydroindenyl, tetrahydroindenyl, indanyl, dihydroindanyl, dihydronaphthyl, tetrahydronaphthyl, naphthyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclobutenyl, cyclopentenyl, cyclohexenyl and the like; heteroaryl and heterocyclyl groups such as pyrrolyl, pyrrolidinyl, furyl, dihydrofuryl, tetrahydrofuryl, furanonyl, benzofuryl, dihydrobenzofuryl, benzofuranonyl, thienyl, benzothienyl, dihydrobenzothienyl, thiazolyl, benzothiazolyl, imidazolyl, benzimidazolyl, pyrazolyl, oxazolyl, isooxazolyl, benzoxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, indolyl, azaindolyl, indolinyl, dihydroindolinyl, dihydroindolinonyl, azaindolinyl, pyranyl, benzopyranyl, dihydrobenzopyranyl, tetrahydrobenzopyranyl, diazinyl, triazinyl, tetrazinyl, pyridyl, piperidinyl, piperidinonyl, pyridazinyl, pyrazinyl, piperazinyl, morpholinyl, quinolinyl, dihydroquinolinyl, oxazinyl, benzoxazinyl, dihydrobenzoxazinyl, thiazinyl,

benzothiazinyl, dihydrobenzothiazinyl, quinazolinyl, dihydroquinazolinyl, phthalazinyl, dihydrophthalazinyl, quinaoxalinyl, dihydrobenzothienyl-1-oxide, dihydrobenzothienyl-1,1-dioxide; heterocyclylcarbonyl groups such as pyrrolidinylcarbonyl, morpholinylcarbonyl, piperidinylcarbonyl, piperazinylcarbonyl and the like, the heterocyclyl group may be substituted; heteroaryl carbonyl group such as pyridylcarbonyl, thienylcarbonyl, furylcarbonyl, pyrrolylcarbonyl, oxazolylcarbonyl, thiazolylcarbonyl, oxadiazolylcarbonyl, thiadiazolylcarbonyl, tetrazolylcarbonyl and the like, the heteroaryl group may be substituted; heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, wherein the heteroaryl and heteroaralkyl moieties are as defined above; aminocarbonyl, which may be substituted; carboxylic acid or its derivatives such as amides, like $CONH_2$, CONHMe, $CONMe_2$, CONHEt, $CONEt_2$, CONHPh and the like. The groups represented by R^4, R^5 and R^6 may be substituted with 1 to 5 substituents.

Suitable substituents on the groups represented by R^4, R^5 and R^6 are selected from halogen atom such as fluorine, chlorine, bromine, or iodine; hydroxy, cyano, nitro, optionally halogenated $(C_1$-$C_6)$alkyl, optionally halogenated $(C_1$-$C_3)$alkoxy, acyl, amino, acylamino, cycloalkyl, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heteroaryloxycarbonylamino, heteroaralkoxycarbonylamino, acyloxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, hydroxyalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, thio, thioalkyl, alkylthio, $(C_1$-$C_6)$alkylsulfinyl, $(C_1$-$C_6)$alkylsulfonyl, sulfonic acid or its derivatives or carboxylic or its derivatives. With a proviso that when the groups R^4, R^5 and R^6 represent phenyl, the phenyl group is not substituted by halogen or hydroxy in the 4^{th} position of the linkage to pyrazole. The substituents are as defined above.

Suitable ring structures formed by pyrazole fused with R^4 may be selected from benzothiopyranopyrazolyl, benzopyranopyrazolyl, benzindazolyl, naphthopyrazolyl,

dihydrobenzindazolyl, dihydronapthopyrazolyl, dihydroindenopyrazolyl, dihydroindanopyrazolyl, benzopiperidinopyrazolyl, benzopiperidinopyrazolyl, pyranopyrazolyl and the like.

The term "pharmaceutically acceptable salts" forming part of this invention include salts derived from inorganic bases such as Li, Na, K, Ca, M, Fe, Cu, Zn, Mn; salts of organic bases such as N,N'-diacetylethylenediamine, betaine, caffeine, 2-diethylaminoethanol, 2-dimethylaminoethanol, N-ethymorpholine, N-ethylpiperidine, glucamine, glucosamine, hydrabamine, isopropylamine, methylglucamine, morpholine, piperazine, piperidine, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine, diethanolamine, meglumine, ethylenediamine, N,N'-diphenylethylenediamine, N,N'-dibenzylethylenediamine, N-benzyl phenylethylamine, choline, choline hydroxide, dicyclohexylamine, benzylamine, phenylethylamine, dialkylamine, trialkylamine, thiamine, aminopyrimidine, aminopyridine, purine, spermidine, and the like; chiral bases like alkylphenylamine, glycinol, phenyl glycinol and the like, salts of natural amino acids such as glycine, alanine, valine, leucine, isoleucine, norleucine, tyrosine, cystine, cysteine, methionine, proline, hydroxy proline, histidine, ornithine, lysine, arginine, serine, threonine, phenylalanine; unnatural amino acids such as D-isomers or substituted amino acids; guanidine, substituted guanidine wherein the substituents are selected from nitro, amino, alkyl, alkenyl, alkynyl, ammonium or substituted ammonium salts and aluminum salts. Salts may include acid addition salts where appropriate which are, sulphates, nitrates, phosphates, perchlorates, borates, hydrohalides, acetates, tartrates, maleates, citrates, succinates, palmoates, methanesulphonates, benzoates, salicylates, hydroxynaphthoates, benzenesulfonates, ascorbates, glycerophosphates, ketoglutarates and the like. Pharmaceutically acceptable solvates may be hydrates or comprising other solvents of crystallization such as alcohols.

Representative compounds according to the present invention are selected from :

4-[5-(4-Methoxy-3-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide ;

4-[5-Phenyl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methylphenyl)-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methylsulfanylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(2-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Dimethylaminophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(2,4-Dimethylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(3-Fluorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(3-Chlorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Isobutylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(2,4-Dimethoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Ethylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(3-Fluoro-4-methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(3,4-Dimethylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Ethoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Ethylsulfanylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(3,4-Dimethoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(2,3-Dihydrobenzothien-5-yl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[3-(4-Methoxyphenyl)-5-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

5-[3-Difluoromethyl-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

5-[3,5-Diphenyl-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

5-[3-Difluoromethyl-5-(4-dimethylaminophenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

5-[3-Trifluoromethyl-5-(4-methylsulfanylphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

5-[3-Difluoromethyl-5-(4-methylsulfanylphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

4-[5-(3-Methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-Thien-2-yl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methylsulfonylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methylsulfanyl-3-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methylsulfanylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

2-Hydroxymethyl-4-(3-trifluoromethyl-4,5-dihydro-1H-benzo[g]indazol-1-yl)-1-benzenesulfonamide ;

4-[5-(3,4-Dimethylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(3-Methyl-4-methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-3-cyano-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Dimethylaminophenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-methoxyphenyl)-3-fluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-3-phenyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(2,3-Dihydrobenzothien-5-yl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-3-(pyridin-3-yl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-3-(furan-2-yl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methylaminophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-3-ethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-3-(pyridin-4-yl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

5-[3-Trifluoromethyl-5-(2,3-dihydrobenzofuran-5-yl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

4-[5-(4-Methoxyphenyl)-4-bromo-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methylsulfonyl-3-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[3,5-Diphenyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

N1-[(Z)-1-Dimethylaminomethylidene]-2-chloromethyl-4-[3-cyano-4-phenyl-1H-pyrazol-1-yl]-1-benzenesulfonamide ;

N1-[(E)-1-Dimethylaminomethylidene]-2-chloromethyl-4-[3-cyano-4-phenyl-1H-pyrazol-1-yl]-1-benzenesulfonamide ;

(Z) 2-Sulfamoyl-5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-benzaldehyde oxime ;

(E) 2-Sulfamoyl-5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-benzaldehyde oxime ;

2-(2,5-Dimethyl-1H-1-pyrrolylsulfonyl)-5-[5-(4-methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]phenyl methanol ;

4-[5-(4-Methoxyphenyl)-3-(pyridin-2-yl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxy-3-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide ;

4-[5-(4-Methylsulfanyl-3-methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methylsulfanylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide ;

4-[5-(2,3-Dihydro-1H-5-indenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide ;

4-[5-Cyclohexen-1-yl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide ;

4-[5-(4-Isobutylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide ;

5-[3-Trifluoromethyl-5-(4-ethoxyphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

5-[3-Trifluoromethyl-5-(3,4-dimethylphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

5-[3-Difluoromethyl-5-(4-methoxy-3-methylphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

5-[3-Trifluoromethyl-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

5-[3-Methyl-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

4-[5-(3,4-Dimethoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methoxymethyl phenyl sulfone ;

4-[5-[4-(Phenyl)phenyl]-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-3-piperidinocarbonyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-Phenyl-4-bromo-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-Phenyl-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-Phenyl-3-cyclohexyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

1-(3-Hydroxymethyl-4-sulfamoylphenyl)-5-phenyl-1H-3-pyrazole carboxamide ;

4-[5-Phenyl-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide;

4-[5-(2,3-Dihydrochroman-6-yl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(3-Chloro-4-methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-Phenyl-3-hydroxymethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

2-Hydroxymethyl-4-[3-trifluoromethyl-1,4-dihydroindeno[1,2-c]pyrazol-1-yl]-1-benzenesulfonamide ;

2-Hydroxymethyl-4-[3-trifluoromethyl-1,8-dihydroindeno[2,1-c]pyrazol-1-yl]-1-benzene sulfonamide ;

Methyl 1-(3-hydroxymethyl-4-sulfamoylphenyl)-5-phenyl-1H-3-pyrazole carboxylate ;

1-(3-Hydroxymethyl-4-sulfomoylphenyl)-5-phenyl-1H-3-pyrazole carboxylic acid ;

4-[5-(3-Methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxy-2,5-dimethylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

Methyl 1-(3-hydroxymethyl-4-sulfamoylphenyl)-3-phenyl-1H-5-pyrazole carboxylate ;

4-[5-(3-Methylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(2,3-Dihydrobenzofuran-5-yl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(2,3-Dihydrobenzofuran-5-yl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(3-Chlorophenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Ethoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-Cyclohexyl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methylsulfanyl-3-methylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Ethylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(4-Methylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-Cyclohexen-1yl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(6-Methoxy-2-naphthyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-Phenyl-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(2,3-Dihydro-1H-5-indenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(1,2,3,4-Tetrahydro-6-naphthalenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(3-Chlorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(2,3-Dihydro-1H-5-indenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-Thien-3-yl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-Furan-2-yl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

4-[5-(3-Fluorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

2-Acetylsulfamoyl-5-[4-bromo-5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-1-yl]benzyl acetate ;

5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-sulfamoylbenzyl propanoate ;

2-Propanoylsulfamoyl-5-[5-phenyl-3-difluoromethyl-1H-pyrazol-1-yl]benzyl propanoate ;

1-(3-Methoxymethyl-4-methylsulfonylphenyl)-5-(4-methylsulfanylphenyl)-3-trifluoromethyl-1H-pyrazole ;

4-[5-(2,3-Dihydro-1H-inden-5-yl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methoxymethyl phenyl methyl sulfone ;

1-(3-Methoxymethyl-4-methylsulfonylphenyl)-5-(cyclohexen-1-yl)-3-trifluoromethyl-1H-pyrazole ;

4-[5-(4-Isobutylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methoxymethyl phenyl methyl sulfone ;

4-[5-(2,4-Dimethoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methoxymethyl phenyl methyl sulfone ;

4-[5-(4-Methylsulfanylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide ;

4-[5-(4-Methoxy-3-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide ;

4-[5-(4-Methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide ;

4-[5-Phenyl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide ;

4-[5-(4-Methoxy-3-chlorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide ;

4-[5-(4-Methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide ;

4-[5-(4-Phenoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

5-[5-(4-Methoxyphenyl)-3-(2-pyridinyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

N-Propanoyl-2-hydroxymethyl-4-(3-trifluoromethyl-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]-1-benzenesulfonamide ;

4-[5-(3-Methyl-4-methoxyphenyl)-3-phenyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide ;

5-[5-(2,3-Dihydrobenzofuran-5-yl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

4-[5-(4-Isobutylphenyl)-3-phenyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide ;

4-[5-(4-Dimethylaminophenyl)-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide ;

4-[5-(3-Methyl-4-methoxyphenyl)-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide ;

1-(3-Hydroxymethyl-4-sulfamoylphenyl)-5-(4-methoxyphenyl)-1H-3-pyrazole carboxamide ;

4-[5-(3-Methyl-4-methoxyphenyl)-3-(2-pyridyl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide ;

5-[5-(6-Methoxy-2-naphthyl)-3-trifluoromethyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

5-[5-(4-Methylsufanylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-sulfamoyl benzyl propanoate ;

5-[5-(2,3-Dihydro-1H-5-indenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate ;

5-[5-(4-Phenoxyphenyl)-3-methyl-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

4-[5-(4-Phenoxyphenyl)-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

2-[1-(3-Hydroxymethyl-4-suflamoylphenyl)-5-(4-methoxyphenyl)-1H-3-pyrazolyl carboxamide]-1,3-thiazole ;

5-[5-(2,3-Dihydro-1H-5-indenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate ;

4-[5-(5-Indenyl)-3-methyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide ;

5-[5-(2,3-Dihydro-1H-5-indenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-sulfamoyl benzyl propanoate ;

5-[5-(4-Phenoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

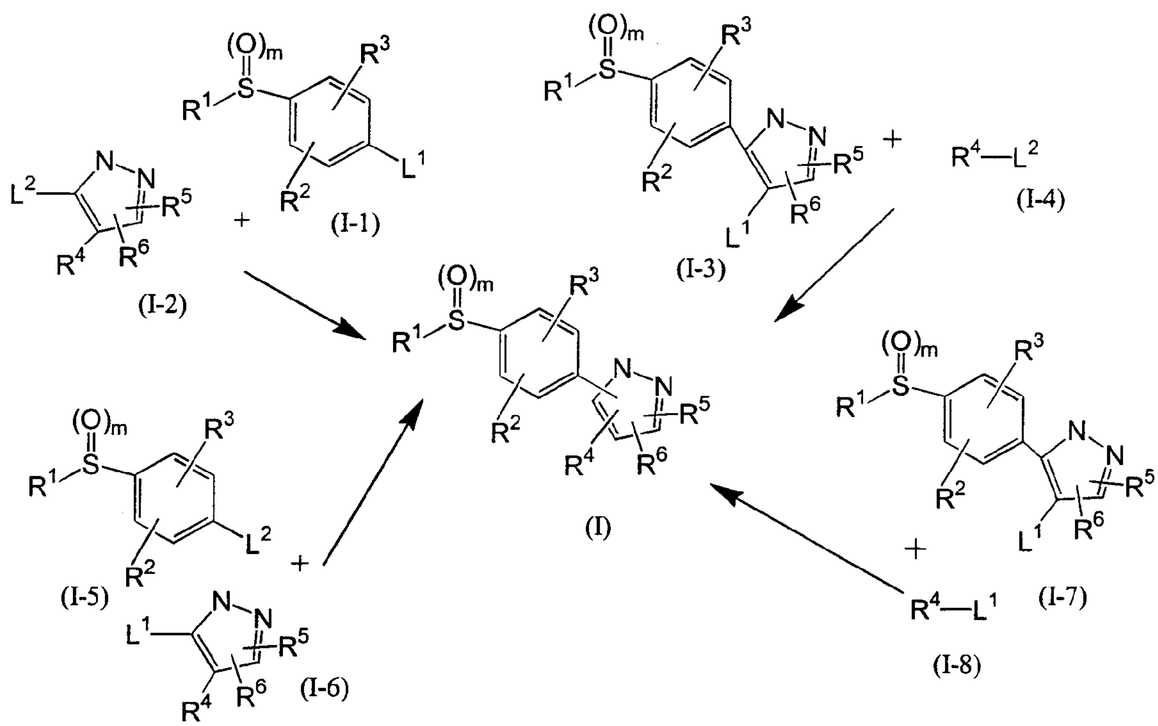
5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methylsulfonyl benzaldehyde ;

5-[5-Phenyl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methylsulfonylphenyl methanol ;

5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate ;

5-[5-(3-Methyl-4-methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate;

According to a feature of the present invention, the compounds of general formula (I) where R^1, R^2, R^3, R^4, R^5, R^6 and m are as defined earlier can be prepared by any of the following routes shown in Scheme - 1 below :

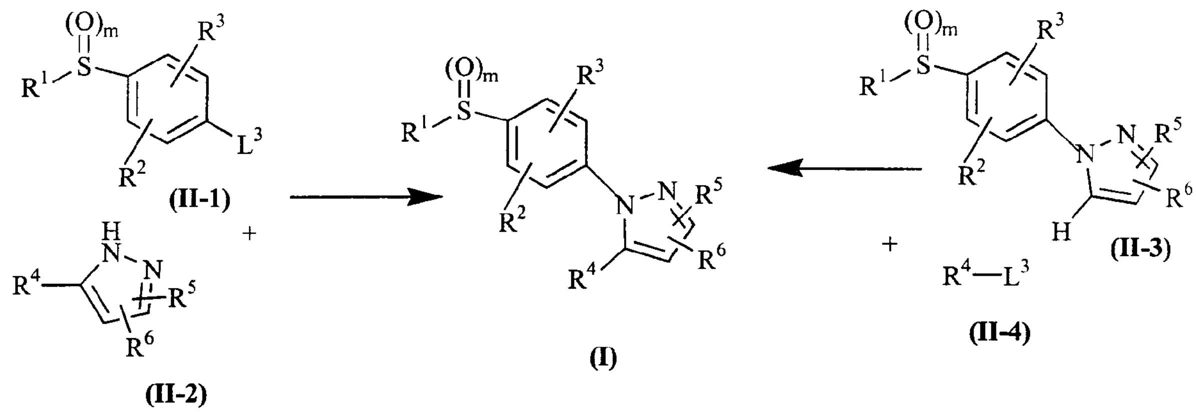


Scheme-1

The reaction of a compound of formula (I-1) with a compound of (I-2) or the reaction of formula (I-3) with a compound of formula (I-4) or the reaction of a compound of formula (I-5) with a compound of formula (I-6) or the reaction of formula (I-7) with a compound of formula (I-8) where L^1 represents $B(OR)_2$, wherein R represents hydrogen or lower alkyl group, L^2 represents halogen atom such as chlorine, bromine or iodine, or other leaving groups such as $ZnCl_2$ or triflate and all other symbols are as defined above to produce a compound of formula (I), where all symbols are as defined above may be carried out in the presence of solvents such as toluene, DMF, dioxane, THF, isopropanol, ethanol, DMSO, DCM, water and the like or mixtures thereof. The reaction may be carried out in an inert atmosphere which may be maintained by using inert gases such as He, N_2, Ar and the like. The reaction may be carried out in the presence of a catalyst such as bis(triphenyl phosphine)palladium(II)chloride, 1,4-bis(diphenyl

phosphine butane)palladium (II)chloride, bis(dibenzylideneacetone)palladium(o), palladium acetate, palladium acetate-tri(o-tolyl)phosphine, bis(acetonitrile)palladium(II)chloride, palladium on carbon + triphenyl phosphine, tetrakis(triphenylphosphine)palladium(o) and the like. The amount of catalyst used may range from 0.1 mol% to 50 mol%, preferably from 1 to 10 mol%. The reaction may be effected in the presence of a base such as alkali metal carbonates like sodium carbonate or potassium carbonate; alkali metal bicarbonates like sodium bicarbonate or potassium bicarbonate; organic bases like triethylamine, pyridine, DMAP or di-isopropylethylamine and the like. The amount of base may range from 1 to 20 equivalents, preferably the amount of base ranges from 1 to 5 equivalents. Phase transfer catalysts such as tetraalkylammonium halide, benzyl triethylammonium halide, benzyl tributylammonium halide, tetraalkylammonium bisulfate, benzyl triethylammonium bisulfate or benzyl tributylammonium bisulfate may be employed. The amount of phase transfer catalyst used may range from 0.01 equivalents to 1 equivalent, preferably from 0.05 to 0.5 equivalents. The reaction temperature may range from 0 °C to reflux temperature of the solvent, preferably from 30 °C to reflux temperature of the solvent. The duration of the reaction may range from 0.5 to 76 hours, preferably from 6 hours to 24 hours.

According to another feature of the present invention, the compounds of general formula (I) where R^1, R^2, R^3, R^4, R^5, R^6 and m are as defined earlier can be prepared by any of the following routes shown in Scheme 2 below :

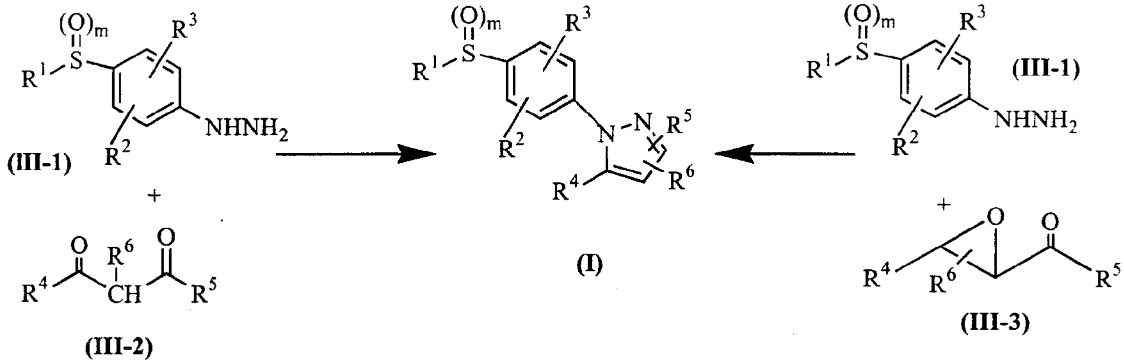


Scheme 2

The reaction of a compound of general formula (II-1) where L^3 represents halogen atom such as fluorine, chlorine, bromine or iodine, and all other symbols are as defined earlier with a compound of formula (II-2) where R^4, R^5 and R^6 are as defined earlier or the reaction of a compound of formula (II-3) where all symbols are as defined earlier with a compound of formula (II-4) where L^3 represents halogen atom such as fluorine, chlorine, bromine or iodine and R^4 is as defined earlier may be carried out in the presence of solvents such as DMSO, DMF, DMA, DME, THF, dioxane, alcohols such as (C_1-C_4) linear or branched alcohols like methanol, ethanol, propanol, isopropanol and the like DCM, acetonitrile, water and the like or mixtures thereof. The reaction may be effected in the presence of a base such as metal hydrides like NaH or KH; organolithiums like CH_3Li or BuLi; alkoxides such as NaOMe, NaOEt, NaOiBu, t-BuOK or sodium amyloxide; alkali metal carbonates like sodium carbonate or potassium carbonate; alkali metal bicarbonate like sodium bicarbonate or potassium bicarbonate; organic bases like TEA, pyridine, DMAP, DIPEA or DBU; hydroxides like NaOH or KOH and the like. The amount of base may range from 1 to 10 equivalents, preferably the amount of base ranges from 1 to 5 equivalents. The reaction may be carried out in an inert atmosphere which may be maintained by using inert gases such as He, N_2, Ar and the like. Phase transfer catalysts such as tetraethylammonium halide, benzyl triethylammonium halide, tetraethylammonium bisulfate, benzyl triethylammonium bisulfate and the like, may be

employed and they may be used in the range of 0.01 to 1.5 equivalents, preferably 0.05 to 0.50 equivalents. The reaction may be more effective under anhydrous conditions. The reaction temperature may be in the range of –78 °C to reflux temperature of the solvent used, preferably at a temperature in the range of 0 °C to reflux temperature of the solvent. The duration of the reaction may range from 1 to 80 hours, preferably from 2 to 50 hours.

According to yet another feature of the present invention, the compounds of general formula (I) where R^1, R^2, R^3, R^4, R^5, R^6 and m are as defined earlier can be prepared by following the routes shown in Scheme 3 below :



Scheme 3

The reaction of a compound of formula (III-1) where all symbols are as defined earlier with a compound of formula (III-2) where R^4, R^5 and R^6 are as defined earlier or R^4 may form a cyclic structure together with the carbon atom adjacent to the carbonyl group which is attached to R^4 or the reaction of a compound of formula (III-1) where all symbols are as defined earlier with a compound of formula (III-3) where R^4, R^5 and R^6 are as defined earlier or R^4 may form a cyclic structure with epoxide carbon adjacent to the carbonyl group to produce a compound of formula (I) where all symbols are as defined earlier may be carried out using solvents such as $(C_1\text{-}C_4)$alcohol like methanol, ethanol, isopropanol and the like; aromatic hydrocarbons like benzene, toluene, xylene and the like; THF, dioxane, DMSO, DMF, DME, DMA, CH_3CN or EtOAc or mixtures thereof. The compound of formula (III-1) may be used as the salts of mineral acids such as HCl, H_2SO_4, and the like or organic acids such as p-toluene, sulfonic acid, acetic acid,

trifluoroacetic acid and the like. The reaction may be carried out in an inert atmosphere which may be maintained by using inert gases such as He, N_2, Ar and the like. The amount of compound of formula (III-2) or (III-3) may range from 1 to 3 equivalents, preferably 1 to 1.5 equivalents. The reaction may be facilitated by azeotropic removal of water using a Dean Stark water separator. The reaction temperature may be in the range of 0 °C to reflux temperature of the solvent used, preferably at a temperature in the range of 20 °C to reflux temperature of the solvent. The duration of the reaction may range from 2 to 20 hours.

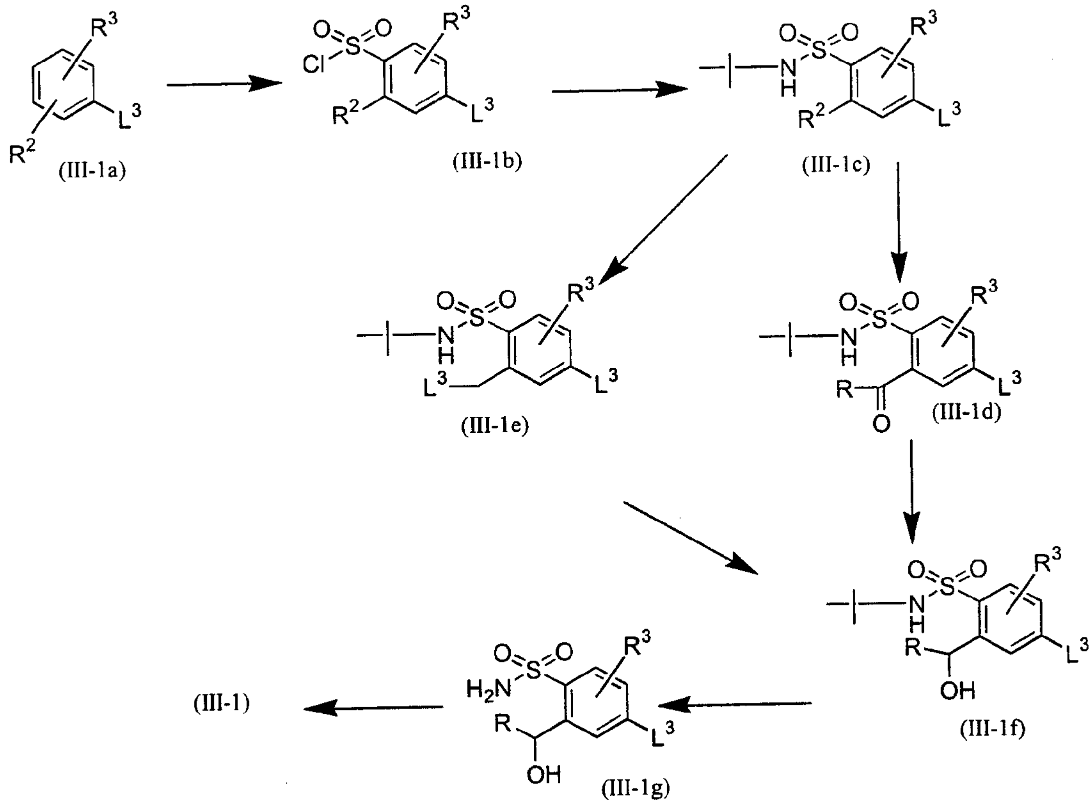
According to another feature of the present invention, the compound of formula (I) where R^1 represents amino group, m represents 2 and all other symbols are as defined above may be prepared by transforming a compound of formula (I) where R^1 represents lower alkyl group, m represents 2 and all other symbols are as defined earlier in the presence of a Grignard reagent like MeMgCl, MeMgBr, EtMgCl or a base such as nBuLi, $LiNH_2$ or LDA. The reaction may be carried out in the presence of trialkyl borane such as triethyl borane or tributyl borane in the presence of a solvent such as dioxane, diethylether, diisobutylether, diphenylether, THF and the like or mixtures thereof. The reaction may be carried out in inert atmosphere which may be maintained by using Ar, N_2 or He. The reaction may be carried out in the temperature range of –78 °C to the reflux temperature of solvent used, preferably at 0 °C to reflux temperature of the solvent used The reaction may be more effective under anhydrous condition. The duration of the reaction may be in the range of 12 to 72 hours, preferably in the range of 15 to 24 hours. The oxidative amination reaction may be carried out in the presence of hydroxylamine-O sulfonic acid and NaOAc. The temperature range of 0 °C to reflux temperature of the solvent, preferably 0 °C to 50 °C may be used. The duration of the reaction may be 2 to 20 hours, preferably 2 to 10 hours.

According to another feature of the present invention the compound of formula (I) where all symbols are as defined earlier and m represents 0 may be prepared by reducing a compound of formula (I) where all symbols are as defined earlier and m represents 1 or 2. The reduction may be carried out using reagents such as LAH, HI,

Bu_3SnH, $TiCl_2$, $MeSiCl_3$, NaI, PCl_3, H_2-Pd-C, acetyl chloride, PPh_3, t-BuBr and tris(dimethylamino)phosphine-I_2. The reduction may also be carried out using diisobutyl aluminium hydride[$(iBu)_2AlH$], LAH according to the procedure described in J.O.C.48,1617(1983).

According to yet another feature of the present invention, the compound of formula (I) where all symbols are as defined earlier and m represents 1 (sulfoxide) or m represents 2 (sulfone) may be prepared by oxidising a compound of formula (I) where all symbols are as defined earlier and m represents 0 with a suitable oxidising agent. The oxidation of a compound of formula (I) where m is 0 may be carried out in the presence of an oxidising agent such as 30 % H_2O_2, m-CPBA, oxone, $NaIO_4$, $KMnO_4$, sodium perborate. The quantity of the reagent varies from 2 mol to 20 mol preferably 4 to 10 mol. The reaction may be effective in presence of a solvent such as $CHCl_3$, t-Butanol, CH_2Cl_2, CH_3COOH, acetone, water and the like or mixtures thereof. Water may be used as cosolvent. The reaction may be carried out in inert atmosphere which may be maintained by using He, N_2 or Ar. The reaction may be carried out at temperature in the range of 0 °C to 150 °C, preferably in the range of 30 °C to 120 °C. The duration of the reaction may range from 0.5 to 24 hours, preferably 0.5 to 12 hours.

In yet another embodiment of the present invention the compound of formula (III-1) where R^1 represents NH_2, R^2 represents linear or branched hydroxyalkyl, alkoxyalkyl or acyl groups; R^3 represents a group inert to the bases such as organolithium and m = 2, can be prepared by the process shown in the Scheme – 4 below.



Scheme-4

The compound of formula (III-1a) where R^2 is hydrogen, L^3 represents halogen atom such as fluorine or chlorine and R^3 is as defined earlier may be converted to a compound of formula (III-1b) where R^2 is hydrogen, L^3 represents halogen atom such as fluorine or chlorine and R^3 is as defined earlier using chlorosulfonic acid either neat or mixed with chlorinated solvents such as chloroform, DCM and the like or mixtures thereof. The amount of chlorosulfonic acid varies from 2 equivalents to 10 equivalents, preferably 3 equivalents to 5 equivalents. The temperature of the reaction may vary from – 20 °C to the reflux temperature of the solvent used, preferably from –10 °C to 30 °C. The duration of the reaction may vary from 0.5 h to 10 h, preferably from 2 h to 5 h. The reaction may be more effective under anhydrous conditions.

The reaction of compound of formula (III-1b) defined above with t-butylamine to produce a compound of formula (III-1c) where R^2 is hydrogen or lower alkyl, L^3

represents halogen atom such as fluorine or chlorine and R^3 is as defined earlier may be carried out neat or in the presence of solvents such as dichloromethane, chloroform, ethyl acetate, toluene benzene, DMF, DME, DMAc, THF, dioxane, DMSO and the like or mixtures thereof. The quantity of t-butylamine may vary from 1 equivalents to 20 equivalents, preferably from 2 – 5 equivalents..The reaction may be carried out in an inert atmosphere which is maintained using inert gases such as N_2, He or Ar. The temperature of the reaction may vary from –10 °C to reflux temperature of the solvent used, preferably from –5 °C to 35 °C. The duration of reaction may range from 1 h to 10 h, preferably from 1 h to 5 h. The reaction may also be carried out using phase transfer catalyst in the quantity ranging from 0.05 to 1.5 equivalent preferably 0.05 equivalent to 1.0 equivalent. The reaction may be more effective under anhydrous conditions.

The conversion of compound of formula (III-1c) where R^2 is hydrogen and other symbols are as defined above to a compound of formula (III-1d) where R represents hydrogen or alkyl group, L^3 represents halogen atom such as fluorine or chlorine and R^3 is as defined earlier may be carried out using organolithium base such as n-butyl lithium, sec-butyl lithium or t-butyl lithium and electrophilic equivalent reagent such as DMF, acid anhydride, DMAc, esters or orthoesters. The quantity of the organo lithium base and the electrophilic equivalent reagent may vary from 1 equivalents to 10 equivalents, preferably from 1.5 equivalents to 3.5 equivalents. The reaction may be carried out in the presence of solvents like diethylether, THF and the like or mixtures thereof. The reaction may be carried out in an inert atmosphere which may be maintained using inert gases such as He, N_2 or Ar. The temperature of the reaction may vary from –78 °C to the reflux temperature of solvent used, preferably from –78 °C to 40 °C. The duration of the reaction varies from 1 h to 50 h, preferably from 2 h to 24 h. The reaction may be more effective under anhydrous conditions.

The conversion of compound of formula (III-1c) where R^2 represents lower alkyl and other symbols are as defined above defined above to a compound of formula (III-1e) where L^3 represents halogen atom such as fluorine or chlorine and R^3 is as defined earlier may be carried out using halogenating agent such as thionyl chloride,

phosphorousoxy chloride, phosphoruspenta chloride, carbon tetra chloride-TPP mixture, N-chlorosuccinimide, N-bromosuccinimide and the like. The quantity of halogenating agent may vary from 0.5 to 2.5 equivalents, preferably, from 0.75 to 1.5 equivalents. The reaction may be carried out in the presence of dry CCl_4, benzene and the like. The reaction may be carried out in an inert atmosphere which may be maintained using inert gases such as He, N_2 or Ar. The reaction may be carried out using radical initiators selected form benzoyl peroxide, light, or 2,2-azobis-isobutyronitrile in the quantity ranging from 0.05 to 1.5 equivalents. The temperature of the reaction may vary from 25 °C to reflux temperature of the solvent used. The duration of the reaction varies from 1 h to 50 h, preferably from 2 h to 24 h. The reaction may be more effective under anhydrous conditions.

The reduction of compound of formula (III-1d) defined above to a compound of formula (III-1f) where R represents hydrogen or alkyl group, L^3 represents halogen atom such as fluorine or chlorine and R^3 is as defined earlier may be carried out using reducing agents such as sodium borohydride, lithium borohydride, Na-Ethanol and the like. The quantity of the reducing agent may vary from 0.25 equivalents to 2.5 equivalents, preferably from 0.25 equivalents to 1 equivalents. The reaction may be carried out in the presence of solvents such as THF, dioxane, alcohol (C_1-C_4, linear or branched) like methanol, ethanol or IPA, water or mixtures thereof. The reaction may be carried out in an inert atmosphere which is maintained by using inert gases such N_2, Ar or He. The temperature of the reaction may range from –20 °C to the reflux temperature of the solvent used, preferably from –10 °C to 50 °C. The duration of the reaction may vary from 0.5 h to 50 h, preferably from 1 h to 20 h. The reaction may be more effective under anhydrous conditions.

Alternatively, the reduction may also be carried out *in situ* after neutralizing the reaction mass (1 g) with 1N-HCl solution at –20 °C to 50 °C.

Alternatively, the compound of formula (III-1f) may be prepared directly from (III-1c). The reaction may be carried out using organo lithium base such as n-butyl lithium, sec-butyl lithium or t-butyl lithium and aldehydes such as paraformaldehyde,

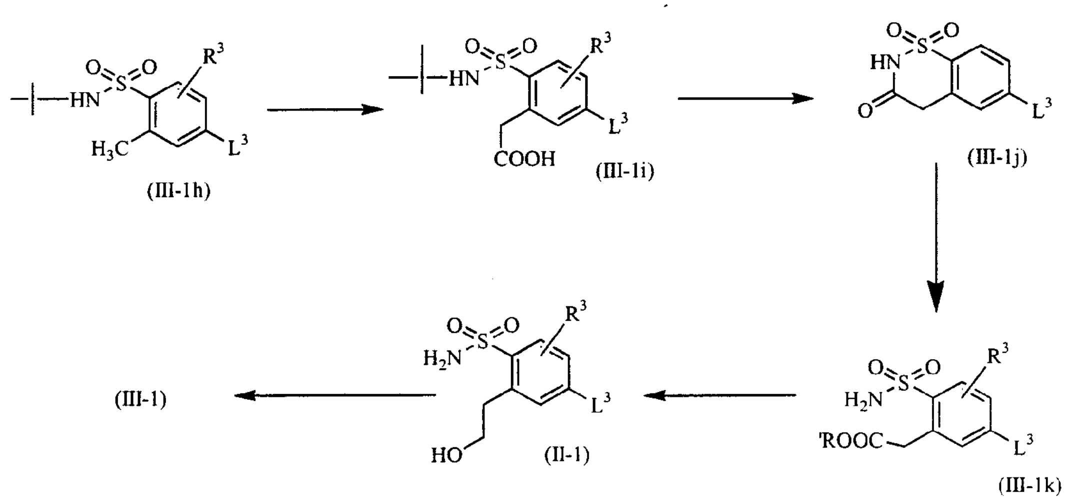
acetaldehyde, methoxyacetaldehyde and the like. The quantity of the organo lithium base and the electrophillic equivalent reagent may vary from 1 equivalents to 10 equivalents, preferably from 1.5 equivalents to 3.5 equivalents. The reaction may be carried out in the presence of solvents like diethylether, THF and the like or mixtures thereof. The reaction may be carried out in an inert atmosphere which may be maintained by using inert gases such as He, N_2 or Ar. The temperature of the reaction may vary from –78 °C to the reflux temperature of solvent used, preferably from –78 °C to 40 °C. The duration of the reaction varies from 1 h to 50 h, preferably from 2 h to 24 h. The reaction may be more effective under anhydrous conditions.

The compound of formula (III-1e) defined above may be converted to a compound of formula (III-1f) using solvents such as acetone, methanol, ethanol and the like or mixtures thereof. The reaction may be effected in the presence of reagents like sodium formate or potassium formate. The quantity of the reagent may vary from 1 equivalent to 20 equivalent, preferably from 2 – 10 equivalents. The reaction may be carried out in an inert atmosphere which is maintained by using inert gases such N_2, Ar or He. The reaction temperature may range from 25 °C to the reflux temperature of solvent used. The duration of the reaction may vary from 1 h to 50 h, preferably from 5 – 20 h and the reaction may be more effective under anhydrous conditions.

The conversion of compound of the formula (III-1f) to a compound of formula (III-1g) may be carried out in the presence of solvents such as benzene, toluene, xylene and the like or mixtures thereof. The reaction may be effected in the presence of an acid catalyst such as p-TSA, TFA, acetic acid, H_2SO_4, HCl and the like. The quantity of the acid catalyst used may vary from 0.05 equivalent to 2.5 equivalent, preferably 0.1 to 1.0 equivalent. The reaction may be carried out in an inert atmosphere which is maintained by using inert gases such N_2, Ar or He. The temperature of reaction may range from 30 °C to the reflux temperature of the solvent used and the duration of the reaction may vary from 1 h to 30 h, preferably from 2 h to 20 h. The reaction may be more effective under anhydrous conditions.

The compound of formula (III-1) where all symbols are as defined above may be prepared by reacting a compound of formula (III-1g) with hydrazine. The reaction may carried out in neat or in the presence of solvents such as DMSO, DMF, acetonitrile, linear or branched (C_1-C_4)alcohol such as methanol, ethanol, isopropanol and the like; DCM, $CHCl_3$, aromatic hydrocarbons such as benzene, toluene or xylene and the like or mixtures thereof. The reaction may be carried out in an inert atmosphere which is maintained by using inert gases such as He, N_2 or Ar. The reaction temperature may range from 20 °C to the reflux temperature of the solvent used. The duration of reaction may vary from 5 h to 100 h, preferably from 20 h to 75 h. The quantity of hydrazine may vary from 1 equivalent to 50 equivalent, preferably 5 – 20 equivalents. The reaction may be more effective under anhydrous conditions.

In yet another embodiment of the present invention the compound of formula (III-1) where R^1 represents NH_2, R^2 represents hydroxyalkyl group, R^3 represents a group inert to the bases like organolithium and m = 2, can also be prepared by a process shown in the Scheme – 5 below :.



Scheme-5

The reaction of a compound of formula (III-1h) where L^3 represents fluorine or chlorine and R^3 is as defined earlier to produce a compound of formula (III-1i) may be carried out using elcetrophilic equivalent reagents such as dry CO_2 in presence of

organo lithium base such as n-butyl lithium, sec-butyl lithium, t-butyl lithium and the like, preferably n-butyl lithium. The reaction may be carried out in the presence of solvents such as dry diethyl ether, THF and the like or mixtures thereof. The quantity of organolithium base may vary from 1 to 5 equivalents, preferably from 1.2 equivalent to 2.5 equivalents. The dry CO_2 slurry may be used in any quantity. The reaction may be carried out in an inert atmosphere which is maintained using inert gases such as He, N_2 or Ar. The reaction temperature may range from range of –78 °C to 40 °C for the period in the range of 1 h to 24 h. The reaction may be more effective under anhydrous conditions. Neutralization with conc. or dilute mineral acids like HCl, H_2SO_4 may be necessary, but it is not essential.

The conversion of compound of the formula (III-1i) defined above to a compound of formula (III-1j) where L^3 represents fluorine or chlorine and R^3 is as defined earlier may be carried out in the presence of solvents such as benzene, toluene, xylene and the like or mixtures thereof. The reaction may be effected in the presence of acid catalysts such as p-TSA, TFA, acetic acid, H_2SO_4, HCl and the like. The quantity of the acid catalyst used may vary from 0.05 equivalent to 2.5 equivalent, preferably 0.1 to 1.0 equivalent. The reaction may be carried out in an inert atmosphere which is maintained by using inert gases such N_2, Ar or He. The temperature of reaction may range from 30 °C to the reflux temperature of the solvent used and the duration of the reaction may vary from 1 h to 30 h, preferably from 2 h to 20 h. The reaction may be more effective under anhydrous conditions.

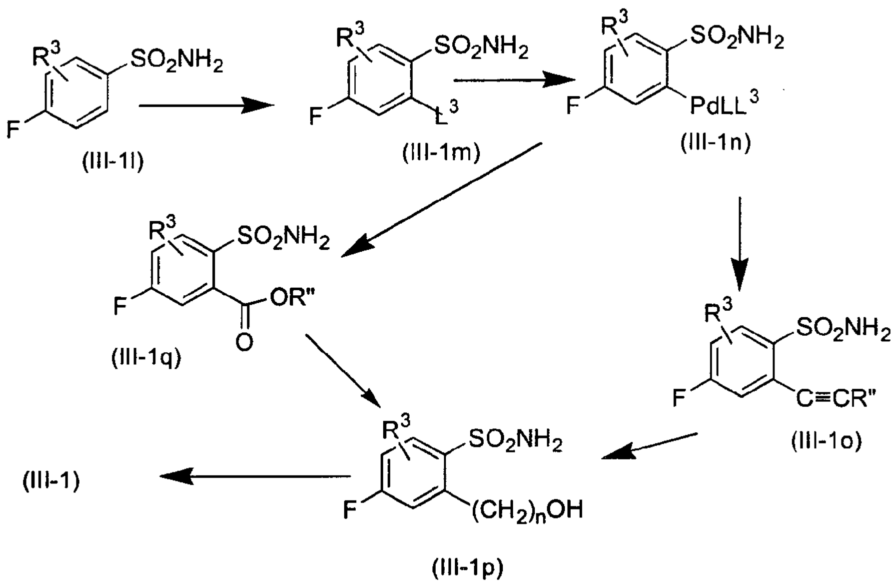
The conversion of compound of formula (III-1j) defined above to an ester of formula (III-1k) where R' represents alkyl group, L^3 represents fluorine or chlorine and R^3 is as defined earlier may be carried out in the presence of alcohol such as (C_1-C_4 linear or branched) alcohol like methanol, ethanol, isopropanol and the like, using metal catalyst such as Zn, Sn and the like or an acid catalyst such as p-TSA, H_2SO_4, HCl, TFA, acetic acid and the like or mixtures thereof. The amount of acid catalyst may vary from 0.05 to 10 equivalents, preferably from 0.05 to 5.0 equivalents. The amount of metal catalyst may vary from 0.01 to 20 equivalents, preferably from 0.01 – 0.50

equivalents. The temperature of the reaction may range from 0 °C to the reflux temperature of the solvent used, preferably from 20 °C to reflux temperature of the solvent. The duration of the reaction may vary from 1 h to 50 h, preferably from 1 h to 24 h. The reaction may be more effective under anhydrous conditions.

The conversion of compound of formula (III-1k) defined above to a compound of formula (II-1) where R^2 represents hydroxyalkyl, L^3 and R^3 are as defined above may be carried out in the presence of solvents such as THF, dioxane, (C_1-C_4 linear or branched) alcohol like methanol, ethanol, isopropanol and the like or mixtures thereof. The reaction may be carried out in the presence of reagents such as lithium borohydride, sodium borohydride and the like or mixtures thereof. The amount of the reagent may range from 0.1 to 5 equivalents, preferably from 0.1 – 2.0 equivalents. The reaction may be carried out in an inert atmosphere which is maintained by using inert gases such N_2, Ar or He. The temperature of the reaction may vary from 0 °C to the reflux temperature of the solvent used and the duration from 1 h to 80 h, preferably from 5 h to 50 h. The reaction may be more effective under anhydrous conditions.

The conversion of compound of formula (II-1) defined above to a compound of formula (III-1) where all symbols are as defined above may be carried out with hydrazine. The reaction may carried out using solvents such as DMSO, DMF, acetonitrile, (C_1-C_4 linear or branched)alcohol such as methanol, ethanol, isopropanol and the like; DCM, $CHCl_3$, aromatic hydrocarbons such as benzene, toluene or xylene and the like or mixtures thereof. The reaction may be carried out in an inert atmosphere which is maintained using inert gases such as He, N_2 or Ar. The reaction temperature may range from 20 °C to the reflux temperature of the solvent used. The duration of reaction may vary from 5 h to 100 h, preferably from 20 h to 75 h. The quantity of hydrazine may vary from 1 equivalent to 50 equivalent, preferably 5 – 20 equivalents. The reaction may be more effective under anhydrous conditions.

In yet another embodiment of the present invention the compound of formula (III-1) where R^1 represents NH_2, R^2 represents hydroxyalkyl, m = 2 and R^3 is as defined earlier may be also prepared by a process shown in Scheme-6 below :



Scheme-6

The compound of formula (III-1m) where all symbols are as defined earlier may be prepared from p-fluoro sulfonylamide of formula (III-1l) using alkyl lithium base such as n-butyl lithium, sec-butyl lithium, t-butyl lithium and the like. The reaction may be carried out in the presence of solvents such as diethylether, THF, and the like or mixtures thereof. The amount of base may vary from 1-10 equivalents, preferably from 1.5 to 3 equivalents. The reaction may carried out in an inert atmosphere which may be maintained using inert gases such as He, Ar, N_2 and the like. The reaction temperature may range from –78 °C to reflux temperature of the solvent used, preferably from –78 °C to 30 °C. The reaction may be quenched with halogen such as iodine or bromine. The quantity of the halogen may vary from 1 to 10 equivalents, preferably from 1.5 to 3 equivalents. Quenching may be carried out in an inert atmosphere at a temperature ranging from –78 °C to reflux temperature of the solvent used, preferably from –78 °C to 30 °C.

The compound of formula (III-1n) where L is a ligand such as triarylphosphine and the like may be prepared by reacting the compound of formula (III-1m) using palladium catalyst such as tetrakis triphenyl phosphine palladium or palladium acetate in the presence of triphenyl phosphine. The amount of catalyst varies from 2 to 20 mol %, preferably from 4-8 mol %. The reaction may be carried out in the presence of a solvent such as DMF, DMSO and the like.

The compound of formula (III-1n) may be coupled with a terminal alkyne to produce a compound of formula (III-1o) where R" represents alkyl, aryl, hydroxyalkyl, alkoxy or alkoxycarbonyl groups and all other symbols are as defined above. The quantity of terminal alkyne may range from 1 to 10 equivalents, preferably from 2 to 5 equivalents. The reaction may be carried out in the presence of a base such as ethylamine, diethylamine, triethylamine and the like. The amount of base may range from 1 to 10 equivalents, preferably from 1.5 to 3 equivalents. The reaction may be carried out in an inert atmosphere which may be maintained using inert gases such as He, Ar, N_2 and the like. The temperature of the reaction may range from 40-150 °C, preferably from 80-120 °C. The reaction may be more effective in the presence of 2-20 mol % copper halide such as CuBr, CuI and the like in the absence of moisture.

The reaction of compound of formula (III-1n) may be carried out under carbon monoxide atmosphere to afford compound of formula (III-1q) where R" represents alkyl, aryl, hydroxyalkyl, alkoxy or alkoxycarbonyl groups and all other symbols are as defined above. The reaction may be carried out in the presence of solvents such as methanol, ethanol, propanol, butanol, and the like. The temperature of the reaction may range from 40-150 °C, preferably from 80-120 °C. The reaction may be more effective under anhydrous conditions.

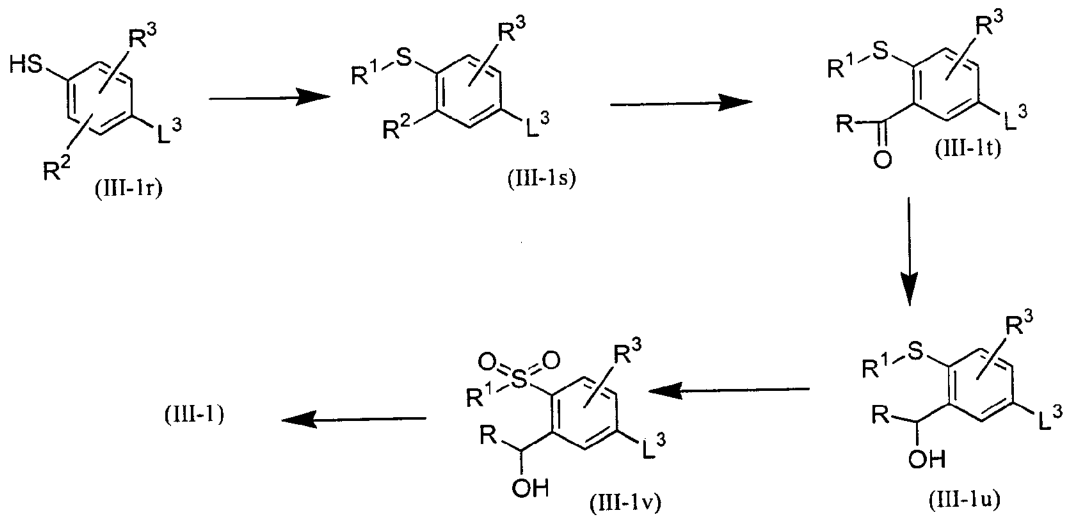
The compound of formula (III-1p) may be produced by reducing the compounds of formula (III-1o) or (III-1q) using suitable reducing agent. The reduction may be carried out in the presence of catalyst such as Raney nickel, palladium/charcoal, platinum or its oxide and the like. The quantity of the catalyst may vary from 5 to 50 % of the amount of the substrate, preferably from 8-20 %. The reaction may effective in the

presence of solvents such as ethyl acetate, methanol, ethanol, isopropanol, butanol, acetic acid, water and the like or mixture thereof. The reduction is carried out under hydrogen atmosphere, the pressure vary from normal atmosphere to 25 psi. The reaction may be more effective in the presence of inert atmosphere which may be maintained by using inert gases such as He, Ar, N_2 and the like. The reaction temperature may range from –78 °C to reflux temperature of the solvent used, preferably from –78 °C to 30 °C.

The reduction of compound of formula (III-1q) to produce compound of formula (III-1p) where n represents 1, and all other symbols are as defined earlier may be carried out using $LiAlH_4$, $LiBH_4$, $NaBH_4$, and the like, in the quantity vary from 2-20 equivalents, preferably from 4-8 equivalents. The reaction may effective in the presence of solvents such as THF, diethylether and the like.

The conversion of compound of formula (III-1p) defined above to a compound of formula (III-1) where all symbols are as defined above may be carried out with hydrazine. The reaction may carried out using solvents such as DMSO, DMF, acetonitrile, (C_1-C_4 linear or branched)alcohol such as methanol, ethanol, isopropanol and the like; DCM, $CHCl_3$, aromatic hydrocarbons such as benzene, toluene or xylene and the like or mixtures thereof. The reaction may be carried out in an inert atmosphere which is maintained by using inert gases such as He, N_2 or Ar. The reaction temperature may range from 20 °C to the reflux temperature of the solvent used. The duration of reaction may vary from 5 h to 100 h, preferably from 20 h to 75 h. The quantity of hydrazine may vary from 1 equivalent to 50 equivalent, preferably 5 – 20 equivalents. The reaction may be more effective under anhydrous conditions.

In another embodiment of the present invention the compounds of formula (III-1) where R^1 represents alkyl group, R^2 represents hydroxyalkyl, R^3 represents a group inert to the bases like organolithium and m is an integer 1 or 2 may be prepared by a process shown in the Scheme – 7 below :



Scheme – 7

The conversion of compound of formula (III-1r) where R^2 is hydrogen, L^3 represents halogen atom such as fluorine, chlorine, bromine or iodine and R^3 is as defined above to a compound of formula (III-1s) where R^1 represents alkyl, R^2 represents hydrogen, R^3 is as defined earlier, may be carried out in neat using alkyl halides or alkyl sulfate. The reaction may be carried out in the presence of solvents such as DMF, DMAc, DMSO, acetone, methanol, ethanol, isopropanol, DME, and the like or mixtures thereof. The reaction may be effective in heterophase using water as a cosolvent. The amount of alkyl halides or alkyl sulfates may vary form 1 to 20, preferably, from 1.5 to 5 equivalents. The reaction may be carried out in the presence of base such as alkyl metal carbonates, bicarbonates, hydroxides and the like, in the quantity ranging form 1 to 10, preferably, from 1.5 to 5 equivalents. The reaction may be carried out at a temperature in the range of 0 to reflux temperature of the solvent used. The duration of the reaction may vary from 1 h to 50 h, preferably from 2 h to 20 h. The reaction may be more effective under anhydrous conditions.

The conversion of compound of formula (III-1s) defined above to a compound of formula (III-1t) where R represents hydrogen or alkyl group, L^3 represents halogen atom such as fluorine, chlorine, bromine or iodine and all other symbols are as defined earlier may be carried out using organolithium base such as n-butyl lithium, sec-butyl lithium

or t-butyl lithium and electrophilic equivalent reagent such as DMF, acid anhydride, DMAc, esters or orthoesters. The quantity of the organo lithium base and the electrophilic equivalent reagent may vary from 1 equivalents to 10 equivalents, preferably from 1.5 equivalents to 3.5 equivalents. The reaction may be carried out in the presence of solvents like diethylether, THF and the like or mixtures thereof. The reaction may be carried out in an inert atmosphere which may be maintained by using inert gases such as He, N_2 or Ar. The temperature of the reaction may vary from –78 °C to the reflux temperature of solvent used, preferably from –78 °C to 40 °C. The duration of the reaction varies from 1 h to 50 h, preferably from 2 h to 24 h. The reaction may be more effective under anhydrous conditions.

The reduction of compound of formula (III-1t) defined above to a compound of formula (III-1u) where R represents hydrogen or alkyl group, L^3 represents halogen atom such as fluorine, chlorine, bromine or iodine and all other symbols are as defined earlier may be carried out using reducing agents such as sodium borohydride, lithium borohydride, Na-ethanol and the like. The quantity of the reducing agent may vary from 0.25 equivalents to 2.5 equivalents, preferably from 0.25 equivalents to 1 equivalents. The reaction may be carried out in the presence of solvents such as THF, dioxane, alcohol (C_1-C_4, linear or branched) like methanol, ethanol or IPA, water or mixtures thereof. The reaction may be carried out in an inert atmosphere, which is maintained by using inert gases such N_2, Ar or He. The temperature of the reaction may range from –20 °C to the reflux temperature of the solvent used, preferably from –10 °C to 50 °C. The duration of the reaction may vary from 0.5 h to 50 h, preferably from 1 h to 20 h. The reaction may be more effective under anhydrous conditions.

The oxidation of compound of formula (III-1u) defined above to produce a compound of formula (III-1v) where L^3 represents fluorine, chlorine, iodine or bromine and all other symbols are as defined above may be carried out using oxidising agents such as hydrogen peroxide, potassium permanganate, m-CPBA, $NaIO_4$, t-BuOCl, sodium perborate, potassium hydrogen persulfate, oxone, $KHSO_5$ and the like. The quantity of oxidising agent used may vary from 1 to 20 equivalents, preferably 2 – 10

equivalents. The reaction may be carried out in the presence of solvents such as glacial acetic acid, propionic acid, acetone, t-butanol, water and the like or mixtures thereof. The reaction may be carried out in an inert atmosphere which is maintained using inert gases such as He, N_2 or Ar. The reaction temperature may range from 20 °C to the reflux temperature of the solvent used, preferably from 50 °C to the reflux temperature of the solvent used. The duration may vary from 15 min to 15 h, preferably from 15 min to 3 h.

The compound of formula (III-1) where all symbols are as defined above may be prepared by reacting a compound of formula (III-1v) with hydrazine. The reaction may carried out in neat or in the presence of solvents such as DMSO, DMF, acetonitrile, linear or branched (C_1-C_4)alcohol such as methanol, ethanol, isopropanol and the like; DCM, $CHCl_3$, aromatic hydrocarbons such as benzene, toluene or xylene and the like or mixtures thereof. The reaction may be carried out in an inert atmosphere which is maintained using inert gases such as He, N_2 or Ar. The reaction temperature may range from 20 °C to the reflux temperature of the solvent used. The duration of reaction may vary from 5 h to 100 h, preferably from 20 h to 75 h. The quantity of hydrazine may vary from 1 equivalent to 50 equivalent, preferably 5 – 20 equivalents. The reaction may be more effective under anhydrous conditions.

It is appreciated that in any of the above mentioned reactions, any reactive group in the substrate molecule may be protected according to conventional chemical practice. Suitable protecting groups in any of the above mentioned reactions are those used conventionally in the art. The methods of formation and removal of such protecting groups are those conventional methods appropriate to the molecule being protected.

The compound of formula (I) when produced through an intermediate compound, conventional functional group transformations such as hydrolysis, reduction or oxidation may be carried out.

The following examples illustrate some of the functional group transformations :

The compounds of formula (I) having $CONH_2$ groups may be transformed to CN by following a procedure disclosed in International publication WO No. 99/15505

The compound of formula (I) where R^1 represents SO_2NH_2 may be transformed to 2,5,dimethyl-1H-pyrazolyl sulfone by following a procedure disclosed in International publication No. WO 96/25405.

Similarly, the compound of formula (I) having CO_2Et group may be transformed to CH_2OH by following a procedure disclosed in International publication No. WO 95/15316.

The pharmaceutically acceptable salts are prepared by reacting the compound of formula (I) or its derivatives with 1 to 4 equivalents of a base such as sodium hydroxide, sodium methoxide, sodium hydride, potassium t-butoxide, calcium hydroxide, magnesium hydroxide and the like, in solvents like ether, THF, methanol, t-butanol, dioxane, isopropanol, ethanol etc. Mixture of solvents may be used. Organic bases like lysine, arginine, diethanolamine, choline, tromethamine, guanidine and their derivatives etc. may also be used. Alternatively, acid addition salts wherever applicable are prepared by treatment with acids such as hydrochloric acid, hydrobromic acid, nitric acid, sulfuric acid, phosphoric acid, p-toluenesulphonic acid, methanesulfonic acid, acetic acid, citric acid, maleic acid salicylic acid, hydroxynaphthoic acid, ascorbic acid, palmitic acid, succinic acid, benzoic acid, benzenesulfonic acid, tartaric acid and the like in solvents like ethyl acetate, ether, alcohols, acetone, THF, dioxane etc. Mixture of solvents may also be used.

The stereoisomers of the compounds forming part of this invention may be prepared by using reactants in their single enantiomeric form in the process wherever possible or by conducting the reaction in the presence of reagents or catalysts in their single enantiomer form or by resolving the mixture of stereoisomers by conventional methods. Some of the preferred methods include use of microbial resolution, resolving the diastereomeric salts formed with chiral acids such as mandelic acid, camphorsulfonic acid, tartaric acid, lactic acid, and the like wherever applicable or chiral bases such as brucine, cinchona alkaloids and their derivatives and the like. Commonly used methods

are compiled by Jaques et al in "Enantiomers, Racemates and Resolution" (Wiley Interscience, 1981).

The regioiosmers of compound of formula (I) may be prepared by modifying the reaction conditions, use of reagents like acid to base or base to acid or by reaction with free base hydrazine instead of its salt with diketone. The molar proportion also can change the regiosiomer formation.

Various polymorphs of compound of general formula (I) forming part of this invention may be prepared by crystallization of compound of formula (I) under different conditions. For example, using different solvents commonly used or their mixtures for recrystallization; crystallizations at different temperatures; various modes of cooling, ranging from very fast to very slow cooling during crystallizations. Polymorphs may also be obtained by heating or melting the compound followed by gradual or fast cooling. The presence of polymorphs may be determined by solid probe NMR spectroscopy, IR spectroscopy, differential scanning calorimetry, powder X-ray diffraction or such other techniques.

The compounds of the general formula (I) are useful as partial or complete substitute for NSAIDS in compositions or preparations wherein they are presently coadministered with other agents or ingredients. The present invention also comprises pharmaceutical compositions for treating cyclooxygenase mediated diseases as defined earlier, comprising a non-toxic therapeutically effective amount of the compound of formula (I) as defined above and pharmaceutically acceptable carrier and optionally containing one or more other therapeutic ingredients such as another analgesic agent like acetaminophen of phenacetin, a potentiator like caffeine, a H_2 antagonist, aluminum or magnesium hydroxide, simethicone, a decongestant such as phenylephrine, phenyl propanolamine, pseudophedrine, oxymetazoline, epinephrine, nephazoline, propylhexadrine or leavo-desoxyephedrine, xylomatazoline, a sedating or non sedating antihistamine, an antitussive such as dextromethorphan, carbetapentane, caramiphen, hydrocodeine and codeine and the like, or a diuretic agent. The present invention also comprises a method of treatment of cyclooxygenase mediated diseases consisting of

administering a patient in need thereof, a nontoxic therapeutically effective amount of compounds of formula (I) or pharmaceutical composition described above.

The pharmaceutical composition containing the active ingredient may be in the form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, hard or soft capsules, or syrups or elixirs. Compositions intended for oral use may be prepared according to any method known to the art for the manufacture of pharmaceutical compositions and such compositions may contain one or more agents selected from the group consisting of sweetening agents, flavouring agents, coloring agents and preserving agents in order to provide pharmaceutically elegant and palatable preparations. Tablets contain the active ingredient in admixture with non-toxic pharmaceutically acceptable excipients which are suitable for the manufacture of tablets. These excipients may be for example, inert diluents, such as calcium carbonate, sodium carbonate, lactose, calcium phosphate or sodium phosphate; granulating and disintegrating agents, for example, corn starch, or alginic acid; binding agents, for example starch, gelatine or acacia, and lubricating agents, for example, magnesium stearate, stearic acid or talc. The tablets may be uncoated or they may be coated by known techniques to delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate may be employed. They may also be coated by the technique described in the U.S. Patent 4,256,108; 4,166,452 and 4,265,874 to form osmotic therapeutic tablets for control release.

Formulations for oral use may also be presented as hard gelatine capsules wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin or as soft gelatine capsules wherein the active ingredients is mixed with water or an oil medium, for example peanut oil, liquid paraffin or olive oil.

Aqueous suspensions contain the active material in admixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients are suspending

agents, for example sodium carboxymethylcellulose, methylcellulose, hydroxypropylmethycellulose, sodium alginate, polyvinyl-pyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents may be a naturally-occurring phosphatide, for example lecithin or condensation products of an alkylene oxide with fatty acids, for example polyoxyethylene stearate or condensation products of ethylene oxide with long chain aliphatic alcohols, for example heptadecaethylene-oxycetanol or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as polyoxyethylene sorbitol monooleate or condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan monooleate. The aqueous suspensions may also contain one or more preservatives, for example ethyl or n-propyl, p-hydroxybenzoate, one or more coloring agents, one or more flavouring agents and one or more sweetening agents, such as sucrose, saccharin or aspartame.

Oily suspensions may be formulated by suspending the active ingredient in a vegetable oil, for example arachis oil, olive oil, sesame oil or coconut oil or in mineral oil such as liquid paraffin. The oily suspensions may contain a thickening agent, for example beeswax, hard paraffin or cetyl alcohol. Sweetening agents such as those set forth above, and flavoring agents may be added to provide a palatable oral preparation. These compositions may be preserved by the addition of an anti-oxidant such as ascorbic acid.

Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient in admixture with a dispersing or wetting agent, suspending agent and one or more preservatives. Suitable dispersing or wetting agents and suspending agents are exemplified by those already mentioned above. Additional excipients, for example sweetening, flavouring and coloring agents, may also be present.

The pharmaceutical compositions of the invention may also be in the form of an oil-in-water emulsions. The oily phase may be a vegetable oil, for example olive oil or arachis oil or a mineral oil, for example liquid paraffin or mixtures of these. Suitable

emulsifying agents may be naturally-occurring phosphatides, for example soy bean, lecithin and esters or partial esters derived from fatty acids and hexitol anhydrides, for example sorbitan monooleate, and condensation products of the said partial esters with ethylene oxide, for example polyoxyethylene sorbitan monooleate. The emulsions may also contain sweetening and flavouring agents.

Syrups and elixirs may be formulated with sweetening agents, for example glycerol, propylene glycol, sorbitol or sucrose. Such formulations may also contain a demulcent, a preservative and flavouring and coloring agents. The pharmaceutical compositions may be in the form of a sterile injectable aqueous or oleagenous suspension. This suspension may be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents which have been mentioned above. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parentally acceptable diluent or solvent, for example as a solution in 1,3-butane diol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono or di glycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

Compounds of formula I may also be administered in the form of a suppositories for rectal administration of the drug. These compositions can be prepared by mixing the drug with a suitable non-irritating excipient which is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum to release the drug. Such materials are cocoa butter and polyethylene glycols.

For topical use, creams, ointments, jellies, solutions or suspensions, etc., containing the compounds of Formula (I) are employed. (For purposes of this application, topical application shall include mouth washes and gargles).

Dosage levels of the order of from about 0.01 mg to about 140 mg/kg of body weight per day are useful in the treatment of the above-indicated conditions or

alternatively about 0.5 mg to about 7 g per patient per day. For example, inflammation may be effectively treated by the administration of from about 0.01 to 50 mg of the compound per kilogram of body weight per day or alternatively about 0.5 mg to about 3.5 g per patient per day, preferably 2.5 mg to 1 g per patient per day.

The amount of active ingredient that may be combined with the carrier materials to produce a single dosage form will vary depending upon the host treated and the particular mode of administration. For example, a formulation intended for the oral administration of humans may contain from 0.5 mg to 5 g of active agent compounded with an appropriate and convenient amount of carrier material which may vary from about 5 to about 95 percent of the total composition. Dosage unit forms will generally contain between from about 1 mg to about 500 mg of an active ingredient, typically 25 mg, 50 mg, 100 mg, 200 mg, 300 mg, 400 mg, 500 mg.

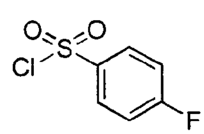
It will be understood, however, that the specific dose level for any particular patient will depend upon a variety of factors including the age, body weight, general health, sex, diet, time of administration, route of administration, rate of excretion, drug combination and the severity of the particular disease undergoing therapy.

The term parenteral as used herein includes subcutaneous injections, intravenous, intramuscular, intrasternal injection or infusion techniques. In addition to the treatment of warm-blooded animals such as mice, rats, horses, cattle sheep, dogs, cats, etc., the compound of the invention is effective in the treatment of humans.

The invention is explained in detail in the examples given below which are provided by way of illustration only and therefore should not be construed to limit the scope of the invention.

Preparation - 1

4-Fluorobenzene sulfonyl chloride:

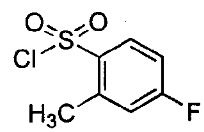


Chloro sulphonic acid (121.56 g, 1.04 mol) was cooled to –5 °C and fluoro benzene (20 g, 0.208 mol) was added very slowly in 1.5 h. The reaction mixture was further stirred at 5-10 °C for 4 h. After completion of the reaction, the reaction mixture was slowly poured into crushed ice (1 kg). After all the ice melts the white solid was filtered and washed with chilled water. The solid was dried in vacuum desicator and chromatographed on silica gel using pet. ether as eluent to yield the title compound (30 g, 74 %), mp 37 – 38 °C.

^{1}HNMR ($CDCl_3$, 200 MHz) δ : 8.11 – 8.09 (m, 2H), 7.34 – 7.25 (m, 2H).

Preparation -2

4-Fluoro-2-methylbenzene sulfonyl chloride

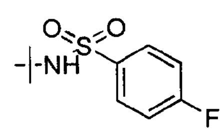


3-Fluorotoluene (20 g, 181.81 mmol) was added slowly (in 1.5 h) to precooled chlorosulfonic acid (63.50 g, 545.45 mmol) solution maintained at –5 to 0 °C under anhydrous conditions and stirred at 0 – 5 °C for 4 h. After completion of the reaction, the reaction mixture was allowed to stand overnight at same temperature. The reaction mixture was poured into ice cold water (500 ml) and stirred and extracted with ethylacetate (3 x 50 ml), dried and evaporated to yield the title compound as viscous liquid (35 g, 92 %).

^{1}H NMR ($CDCl_3$, 200 MHz) δ : 8.10 (m, 1H), 7.10 (m. 2H), 2.79 (s, 3H).

Preparation – 3

4-Fluoro-N-t-butylbenzene sulfonamide:



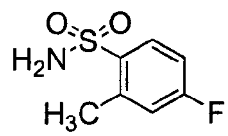
A solution of 4-fluorobenzenesulfonyl chloride (10 g, 51.41 mmol) obtained in preparation 1 in dichloromethane (100 ml) was cooled to 0 - 5 °C and t-butylamine (13.13 g, 179.9 mmol) was added slowly. The reaction mixture was stirred for 1 hr at 5 –

10 °C and water was added and extracted with dichloromethane (2 x 100 ml). The combined dichloromethane layers were washed with water, brine, dried (Na_2SO_4) and the solvent was evaporated under reduced pressure to yield the solid product, which was crystallized from pet. ether to afford the title compound (11.5 g, 97 %), mp 84 – 88 °C.

^{1}HNMR ($CDCl_3$, 200 MHz) δ : 7.94 – 7.87 (m, 2H), 7.19 – 7.11 (m, 2H), 4.92 (bs, D_2O exchangeable, 1H), 1.21 (s, 9H).

Preparation-4

4-Fluoro-2-methylbenzene sulfonamide

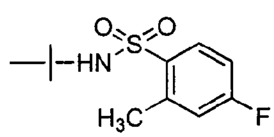


To a cooled solution of 4-fluoro-2-methylbenzene sulfonyl chloride (14.0 g, 67 mmol) obtained in preparation 2 in dioxane (30 ml) aqueous ammonia solution (25 %, 140 ml) was added, with stirring. The mixture was stirred for 6.0 h at 0 °C. The separated solid was filtered and washed with cold water (100 ml) to yield the title compound as a white solid (10.0 g, 79.0 %), mp 178-180 °C.

^{1}H NMR (DMSO-d^6, 200 MHz) δ : 7.90 (m, 1H), 7.40 (s, D_2O exchangeable, 2H), 7.20 (m, 2H), 2.59 (s, 3H).

Preparation – 5

4-Fluoro-2-methyl N-t-butylbenzene sulfonamide :



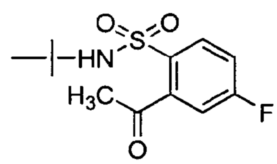
To a solution of 4-fluoro-2-methylbenzene sulfonyl chloride (20 g, 95.92 mmol), obtained in preparation 4 taken in DCM (150 ml), cooled to 0 – 5 °C and t-butylamine (24.5 g, 335.73 mmol) was slowly added in 2 h. The reaction mixture was stirred at 20 – 25 °C for 2 h and poured in water (500 ml). After stirring for 10 – 15 min, the DCM layer was separated and water layer extracted with DCM (2 x 100 ml). The combined

organic layers were dried (Na_2SO_4) and evaporated. The residue was triturated with pet. ether to yield the title compound as white solid (22.5 g, 98 %), mp 138-140 °C.

^{1}HNMR ($CDCl_3$, 200 MHz) δ : 8.10 – 8.00 (m, 1H), 7.08 – 6.95 (m, 2H), 4.60 (bs, D_2O exchangeable, 1H), 2.65 (s, 3H), 1.22 (s, 9H).

Preparation – 6

4-Fluoro-2-acetyl N-t-butylbenzene sulfonamide :

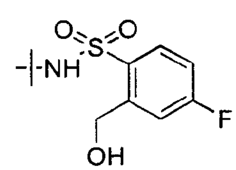


To a solution of 4-fluoro N-t-butylbenzene sulfonamide (2 g, 8.65 mmol) obtained in preparation 3 taken in dry THF (20 ml) under argon atmosphere was cooled to –78 °C and n-butyl lithium (20 ml, 26.2 mmol) was slowly added and stirred for 1 h. To this reaction mixture acetic anhydride (2.1 ml, 21.65 mmol) was added slowly. The reaction temperature was maintained at –78 °C for 1 h and brought to room temperature and stirred for further 15 h. After completion of the reaction, the reaction mixture was quenched with saturated NH_4Cl solution (100 ml), pH adjusted to 6-7 by 1N HCl and extracted with ethyl acetate (3 x 50 ml), dried, evaporated and chromatographed over silica gel column using mixture of ethyl acetate : pet. ether (10 : 90) to yield the title compound as viscous liquid (2.00 g, 85 %).

^{1}HNMR ($CDCl_3$, 200 MHz) δ : 8.15 – 8.05 (m, 1H), 7.30 – 7.15 (m, 2H), 5.21 (bs, D_2O exchangeable, 1H), 2.62 (s, 3H), 1.22 (s, 9H).

Preparation 7

4-Fluoro-2-hydroxymethyl N-t-butyl-1-benzene sulfonamide :



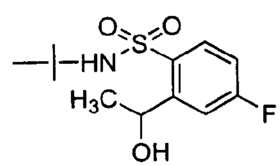
A solution of 4-fluoro-N-t-butylbenzene sulfonamide (500 mg, 2.16 mmol) obtained in preparation 3 in perfectly dry THF under argon atmosphere was cooled to -

78 °C and n-butyl lithium (3.24 ml, 1.4 M, 4.53 mmol) was slowly injected. The reaction mixture was stirred for 1 hr at -78 °C and dry DMF (0.42 ml, 5.34 mmol) was slowly added and stirring was continued for further 2 h. The reaction mixture was allowed to room temperature and stirring was continued for further 24 h. The reaction mixture was re-cooled to 0 – 5 °C and neutralized to pH 7.0 - 8.0 with 1N HCl and sodium borohydride (120 mg, 3.2 mmol) was slowly added and stirred for further 1 hr. The solvent was evaporated and the residue was suspended in water and extracted with ethyl acetate (25 ml). The combined ethyl acetate extracts were dried (Na_2SO_4), filtered and the solvent was evaporated to yield the crude compound. The crude compound was triturated with ether to yield the title compound (508 mg, 90 %), mp 148 °C.

^{1}HNMR ($CDCl_3$, 200 MHz) δ : 8.06 – 7.99 (m, 1H), 7.31 – 7.26 (m, 1H), 7.12 – 7.03 (m, 1H), 5.01 – 4.97 (m, 1H D_2O exchangeable, 3H), 1.22 (s, 9H).

Preparation – 8

4-Fluoro-2-(1-hydroxyethyl) N-t-butyl-1-benzene sulfonamide

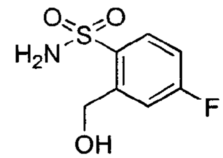


The 4-fluoro-2-acetyl N-t-butylbenzene sulfonamide (2 g, 7.32 mmol), obtained in preparation 6 in methanol (20 ml) was cooled to 0 °C and sodium borohydride (140 mg, 3.78 mmol) was slowly added and stirred at 20 – 25 °C for 4 h. After completion of the reaction, methanol was evaporated, water (50 ml) was added and extracted with ethyl acetate (3 x 25 ml). The combined organic layers were washed with brine, water, dried (Na_2SO_4) and evaporated to yield the title compound as viscous liquid (1.95 g, 95 %).

^{1}HNMR ($CDCl_3$, 200 MHz) δ : 8.10 – 8.00 (m, 1H), 7.50 – 7.40 (m, 1H), 7.15 – 7.00 (m, 1H), 5.70 (q, J = 6.40 Hz, 1H), 1.58 (d, J = 6.20 Hz, 3H), 1.35 (s, 9H).

Preparation 9

4-Fluoro-2-hydroxymethyl-1-benzene sulfonamide:

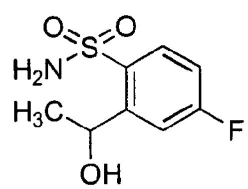


A solution of 4-fluoro-2-hydroxymethyl N-t-butylbenzene sulfonamide (250 mg, 0.95 mmol) obtained in preparation 7 in benzene (10 ml) with p-toluene sulfonic acid (18 mg, 0.09 mmol) was refluxed azeotropically for 8 h, cooled, removed benzene and ethylacetate (20 ml) was added. The organic layer was washed with cold solution of 2 % sodium bicarbonate (2 x 10 ml), water (20 ml), dried (Na_2SO_4), filtered and the solvent was removed under reduced pressure to yield a solid which on trituration with ether yielded the compound (185 mg, 94 %), mp 122 – 124 °C.

^{1}HNMR (DMSO–d_6, 200 MHz) δ : 7.95 – 7.85 (m, 1H), 7.60 (d, J = 10.4 Hz, 1H), 7.50 (bs, D_2O exchangeable, 2H), 7.30 – 7.20 (m, 1H), 5.65 (bs, D_2O exchangeable, 1H), 4.92 (d, J = 4.00 Hz, 2H); ^{13}C NMR (DMSO–d_6, 50 Hz) δ : 185.4, 166.7, 161.8, 144.9, 144.7, 136.4, 130.3, 130.1, 114.4, 113.9, 113.5, 113.1, 59.5; Mass (m/z, relative intensity) 189, 170, 159, 143, 123, 95.

Preparation – 10

4-Fluoro-2-(1-hydroxyethyl)-1-benzene sulfonamide

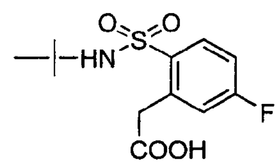


To 2-(1-hydroxyethyl)-4-fluoro-N-t-butyl-benzene sulfonamide (1.5 g, 5.45 mmol) obtained in preparation 8, taken in benzene (25 ml), p-toluene sulfonic acid (100 mg) was added and refluxed for 24 h using Dean stark apparatus. After completion of reaction, the reaction mixture was poured into water (25 ml), extracted with ethyl acetate (3 x 20 ml) and washed with 5 % $NaHCO_3$ solution (15 ml) followed by water (50 ml). After drying (Na_2SO_4) the organic layers were evaporated to yield gummy mass which was chromatographed on silica gel column using ethyl acetate : pet. ether (20 : 80) to yield the title compound as viscous liquid (1 g, 84 %).

[1]HNMR ($CDCl_3$, 200 MHz) δ : 8.15 – 8.02 (m, 1H), 7.40 – 7.30 (m, 1H), 7.20 – 7.04 (m, 1H), 5.68 (q, J = 6.60 Hz, 1H), 3.00 (bs, D_2O exchangeable, 3H), 1.64 (d, J = 6.40 Hz, 3H).

Preparation – 11

5-Fluoro-2-(N-t-butyl sulfamoyl)phenyl acetic acid

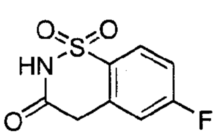


To a solution of 2-methyl-4-fluoro-N-t-butylbenzenesulfonamide (5g, 20.40 mmol) obtained in preparation 5 dissolved in dry THF (40 ml) under argon atmosphere was cooled to –78 °C and n-butyl lithium solution in hexane (30.1 ml, 1.4 M, 42.14 mmol) was added slowly and stirred for 1 h. The reaction mixture was slowly allowed to attain room temperature and stirred for 2 h. The reaction mixture was poured into the premade slurry of dry ice in THF (30 g in 100 ml) and stirred for 2 h. Water (100 ml) was added followed by sufficient conc. HCl to bring the pH to 4-5. Extracted with ethyl acetate (3 x 100 ml), dried (Na_2SO_4) and evaporated to yield viscous liquid which upon trituration with pet. ether afforded the title compound as white solid (5.20 g, 88 %), mp 118-120 °C.

[1]HNMR ($CDCl_3$, 200 MHz) δ : 8.15 – 8.02 (m, 1H), 7.20 – 7.02 (m, 2H), 5.00 – 4.70 (bs, D_2O exchangeable, 2H), 4.15 (s, 2H), 1.22 (s, 9H).

Preparation – 12

6-Fluoro-1,1,3-trioxo-3,4-dihydro-1,2-benzothiazine



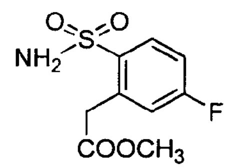
To a solution of 5-Fluoro-2-(N-t-butyl sulfamoyl)phenyl acetic acid (5g, 17.30 mmol) obtained in preparation 11 in benzene (50 ml), p-toluene sulphuric acid (330 mg, 1.73 mmol) was added and refluxed using Dean-stark separator for 4h. After completion of reaction, the reaction mixture was cooled to room temperature, water was added,

separated the organic layers and extracted the aqueous layers again with ethyl acetate (2 x 25 ml). The combined organic layers were washed with 2.5 % $NaHCO_3$ solution (2 x 10 ml), dried (Na_2SO_4) and evaporated to yield solid which was filtered and washed with pet. ether to yield the title compound (3.5 g, 94 %), mp 218-220 °C.

^{1}HNMR (DMSO-d_6, 200 MHz) δ : 8.05 – 7.90 (m, 1H), 7.60 – 7.40 (m, 2H), 4.50 (bs, D_2O exchangeable, 1H), 4.10 (s, 2H).

Preparation –13

4-Fluoro-2-methylcarboxymethylbenzene sulfonamide

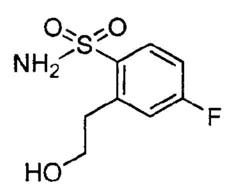


6-Fluoro-1,1,3-trioxo-3,4-dihydro-1,2-benzothiazine (3g, 13.95 mmol) obtained in preparation 12 was dissolved in methanol (20 ml) and conc. HCl (3.0 ml, 3.0 mmol) and Zn dust (0.065 g, 1 mmol) was added. The reaction mixture was refluxed for 2 h and methanol was removed under reduced pressure. Water (50 ml) was added to the residue and extracted with ethyl acetate (3 x 20 ml). The ethyl acetate layers were washed with 5 % $NaHCO_3$ solution (2 x 10 ml), dried (Na_2SO_4) and evaporated to yield viscous liquid which on trituration with pet. ether afforded the title compound (3.20 g, 93 %), mp 112-114 °C.

^{1}HNMR ($CDCl_3$, 200 MHz) δ : 8.18 – 8.06 (m, 1H), 7.20 – 7.00 (m, 2H), 5.40 (bs, D_2O exchangeable, 2H), 4.20 (s, 2H), 3.75 (s, 3H).

Preparation – 14

4-Fluoro-2-hydroxyethylbenzene sulfonamide



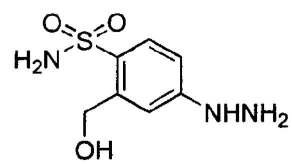
To 4-fluoro-2-methylcarboxymethylbenzene sulfonamide (3.0 g, 12.14 mmol) obtained in preparation 13 dissolved in dry THF (30 ml) and lithium borohydride (121

mg, 6.07 mmol) was added portion wise at 20 – 25 °C. The reaction mixture was refluxed for 7 h and THF was evaporated. The residue was treated with water, neutralized with 1N HCl and extracted with ethyl acetate (3 x 25 ml). The combined organic layers were washed with water, dried (Na_2SO_4) and evaporated to yield residue which on column purification using ethyl acetate pet. ether (30 : 70) afforded the title compound (2.5 g, 94 %), mp 97-98 °C.

^{1}HNMR ($CDCl_3$, 200 MHz) δ : 8.12 – 8.05 (m, 1H), 7.18 – 7.00 (m, 2H), 5.45 (bs, D_2O exchangeable, 2H), 4.05 (t, J = 5.80 Hz, 2H), 3.40 (t, J = 5.80 Hz, 2H).

Preparation 15

3-Hydroxymethyl-4-hydrazinobenzene sulfonamide

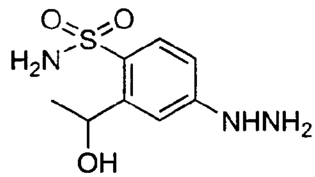


A solution of 4-fluoro-2-hydroxymethylbenzene sulfonamide (5g, 24.39 mmol) obtained in preparation 9 in dry acetonitrile (50 ml), anhydrous hydrazine (7.8 ml, 243.90 mmol) was added under argon atmosphere and refluxed for 30 - 40 h. Solvent was removed under reduced pressure and distilled water (25 ml) was added under stirring. The reaction mixture was slowly cooled to a temperature of 5 - 10 °C and stirred for 2 h, filtered and washed with chilled water to yield the title compound (5 g, 95 %), mp 160 – 162 °C.

^{1}HNMR ($CDCl_3$, 200 MHz) δ : 7.58 (d, J = 8.72 Hz, 1H), 7.45 (s, D_2O exchangeable, 1H), 7.08 (s, 1H), 6.95 (s, D_2O exchangeable, 2H), 6.72 (d, J = 6.60 Hz, 1H), 5.31 (t, J = 5.40 Hz, 1H D_2O exchangeable), 4.82 (d, J = 4.90 Hz, 2H), 4.20 (bs, D_2O exchangeable, 2H).

Preparation – 16

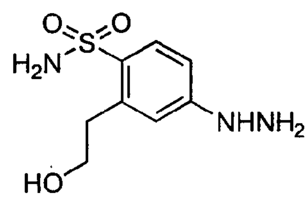
4-Hydrazino-2-(1-hydroxyethyl)benzene sulfonamide



A solution of 4-fluoro-2-(1-hydroxyethyl)benzene sulfonamide (5g, 24.39 mmol) obtained in preparation 10 in dry acetonitrile (50 ml), anhydrous hydrazine (7.8 ml, 243.90 mmol) was added under argon atmosphere and refluxed for 30 - 40 h. Solvent was removed under reduced pressure and distilled water (25 ml) was added under stirring. The reaction mixture was slowly cooled to a temperature of 5 - 10 °C and stirred for 2 h, filtered and washed with chilled water to yield the title compound (2.95 g, 56 %) which was used directly in the next step.

Preparation – 17

4- Hydrazino-2-(2-hydroxyethyl)benzene sulfonamide

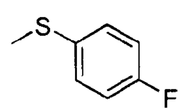


The title compound (1.75 g, 83 %) was prepared from 4-fluoro-2-hydroxyethylbenzene sulfonamide (2 g, 9.13 mmol) obtained in preparation 14 by a procedure similar to that described in preparation 15, mp 128-129 °C.

^{1}HNMR ($CDCl_3$, 200 MHz) δ : 7.57 (d, J = 8.60 Hz, 1H), 7.29 (s, 1H), 6.95 (s, D_2O exchangeable, 2H), 6.69 (s, D_2O exchangeable, 1H), 6.63 (d, J = 8.80 Hz, 1H), 4.68 (t, J = 5.20 Hz, D_2O exchangeable, 1H), 4.11 (bs, D_2O exchangeable, 2H), 3.66 (t, J = 5.40 Hz, 2H), 3.03 (t, J = 7.00 Hz, 2H).

Preparation 18

4-Fluoro-1-methylsulfanyl benzene :

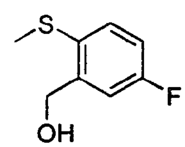


To a solution of 4-fluorothiophenol (25 g, 195.05 mol) in dry acetone (500 ml), dry K_2CO_3 (80.8 g, 584.74 mmol) was added and stirred the mixture at room temperature for 1 h. The mixture was cooled to 0 – 5 °C and methyliodide (84.26 g, 585 mmol) was slowly added and stirred the mixture at 0-5 °C for 1h. The reaction mixture was further stirred at room temperature for 24 h. The reaction mixture was filtered and washed with acetone. The filtrate was concentrated, dichloromethane was added and washed with water. The organic layer was concentrated washed with water and concentrated to yield the title compound as light yellow viscous liquid (25 g, 90 %).

^{1}HNMR ($CDCl_3$, 200 MHz) δ : 7.28 – 7.21 (m, 2H), 7.03 – 6.95 (m, 2H), 2.46 (s, 3H).

Preparation -19

5-Fluoro-2-methyl sulfanyl phenyl methanol

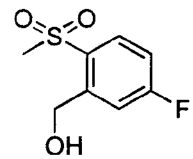


Dry THF (250 ml) was added under argon atmosphere to 4-fluoro-1-methylsulfanyl benzene (12 g, 84.5 mmol) obtained in preparation 18 slowly and cooled to –78 °C. n-Butyl lithium (85 ml, 15 % in hexane, 126.7 mmol) was slowly injected to the reaction vessel with canula and stirred for 1 h at this temperature. Dry dimethyl formamide (16.4 ml, 211.0 mmol) was added slowly to the reaction mixture at –78 °C and stirred for further 1h. Then, the reaction mixture was poured into ice water, added with con. HCl (10 ml), stirred well and pH wass adjusted to 7 -8. Solid sodium borohydride (9.68 g, 254.7 mmol) was added and continued the stirring for 10 min. The reaction mixture was extracted with ethyl acetate (3 x 200 ml), concentrated and purified by column chromatography using 10-15 % ethyl acetate – pet. ether as eluent to yield the title compound as viscous liquid (10 g, 69 %).

^{1}H NMR ($CDCl_3$, 200 MHz) δ : 7.35 (dd, J = 2.00 and 8.00 Hz, 1H), 7.21 – 7.14 (m, 1H), 6.97 (t, J = 9.00 Hz, 1H), 4.73 (s, 2H), 2.47 (s, 3H), 1.8 (bs, D_2O exchangeable, 1H).

Preparation -20

5-Fluoro-2-methyl sulfonyl phenyl methanol

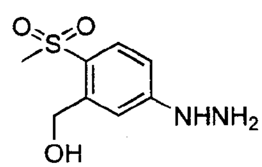


To 5-fluoro-2-methyl sulfanyl phenyl methanol (10 g, 58.3 mmol) obtained in preparation 19 taken in acetone-water (50 : 50 ml) mixture was added oxone (71.5 g, 116.3 mmol) and stirred at room temperature for over night. The reaction mixture was poured into ice water, stirred and extracted with ethyl acetate. The solvent was evaporated and the residue was purified by column chromatography using 20 – 30 % ethyl acetate – pet. ether as eluent to yield the title compound as a white solid (6.45 g, 54 %), mp 103 – 106 °C.

^1H NMR ($CDCl_3$, 200 MHz) δ : 8.09 – 8.06 (m, 1H), 7.88 – 7.80 (m, 1H), 7.25 – 7.14 (m, 1H), 4.80 (s, 2H), 3.04 (s, 3H), 2.62 (bs, D_2O exchangeable, 1H).

Preparation -21

5-Hydrazine-2-methyl sulfonyl phenyl methanol

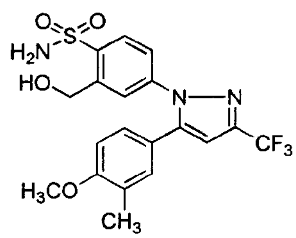


To 5-fluoro-2-methyl sulfonyl phenyl methanol (3 g, 14.70 mmol) obtained in preparation 20 taken in acetonitrile (40 ml) was added anhydrous hydrazine (4 ml) under argon atmosphere and refluxed for 60 h. Acetonitrile and excess hydrazine were removed completely and distilled water (10 ml) was added under vigorous shaking. The solution was kept in freezer for 4 h and shaken well to obtain a white solid precipitate. The precipitate was filtered and washed with water (5 ml) followed by ethyl acetate (5 ml) to yield the title compound as a while solid (2.8 g, 88 %), mp 156 – 158 °C.

^1H NMR ($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 7.72 – 7.58 (m, 1H), 7.30 (d, J = 8.60 Hz, 1H), 7.02 (s, 1H), 5.05 (bs, D_2O exchangeable, 1H), 4.56 (s, 2H), 3.90 (bs, D_2O exchangeable, 2H), 3.04 (s, 3H).

Example 1

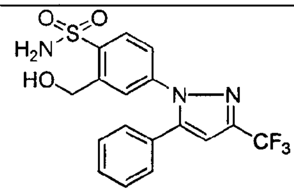
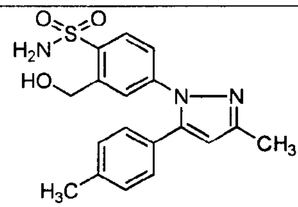
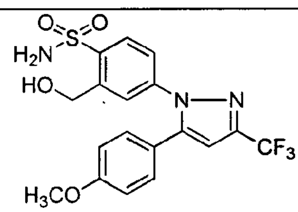
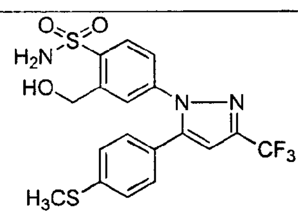
4-[5-(4-Methoxy-3-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethylbenzene sulfonamide

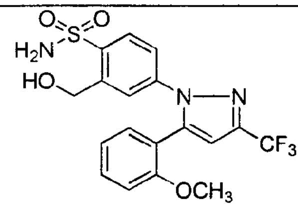
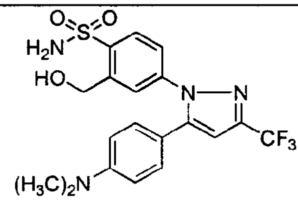
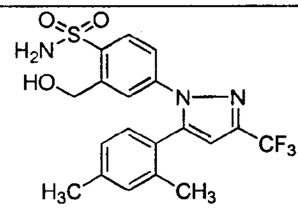
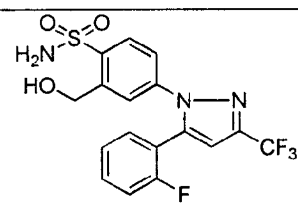
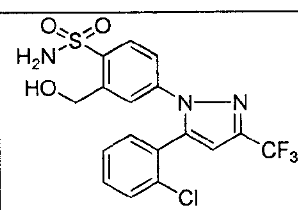


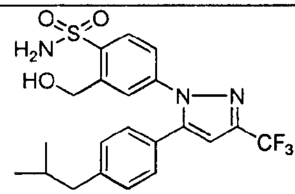
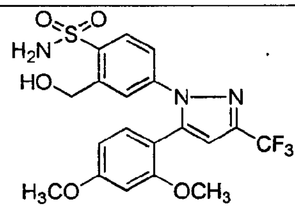
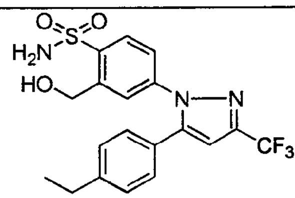
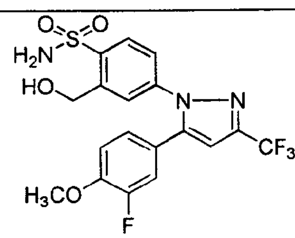
To a solution of 2-hydroxymethyl-4-hydrazine-1-benzenesulfonamide (100 mg, 0.46 mmol) obtained in preparation 15 in methanol (5 ml) was added isopropanol and hydrochloric acid till pH 2.5 with stirring. The solvent was evaporated completely at 40-50 °C to obtain solid product. The solid product obtained was dissolved in ethanol (10 ml), 4-methoxy-3-methyl-1,3-diketone (126 mg, 0.48 mmol) was added and refluxed for 10 h. The solvent was removed and the residue treated with chilled (0-5 °C) solution of dilute sodium bicarbonate till pH 7.5-8.0. The residue was extracted with ethylacetate (3 x 10 ml), washed with water, dried (Na_2SO_4), evaporated and chromatographed over silica gel column using 30 % ethyl acetate and pet. ether as an eluent to yield the title compound (195 mg, 96 %). mp. 156 – 158 °C.

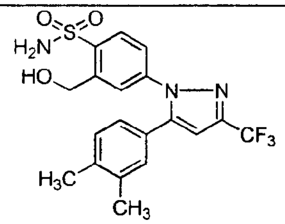
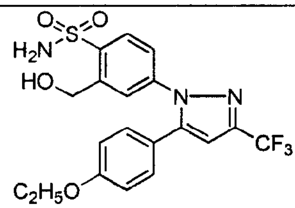
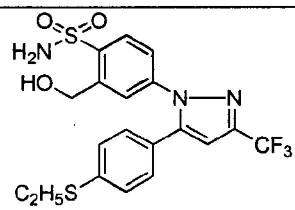
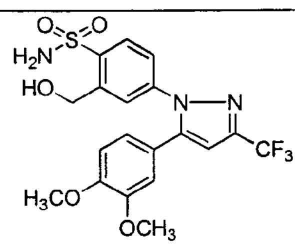
($CDCl_3$, 200 MHz) δ : 7.98 (d, J = 8.60 Hz, 1H), 7.66 (d, J = 2.20 Hz, 1H), 7.28 (s, 1H), 7.10 (s, 1H), 6.91 (d, J = 2.00 Hz, 1H), 6.74 (d, J = 8.40 Hz, 1H), 6.70 (s, 1H), 5.42 (bs, D_2O exchangeable, 2H), 5.04 (s, 2H), 3.85 (s, 3H), 2.65 (bs, D_2O exchangeable, 1H), 2.20 (s, 3H).

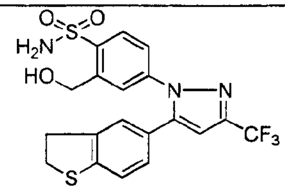
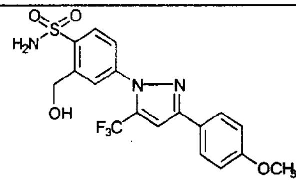
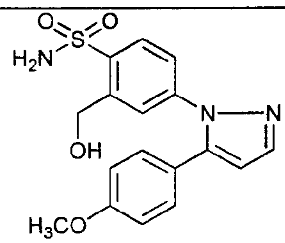
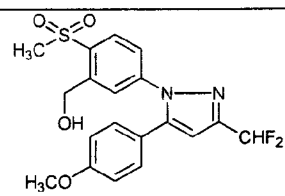
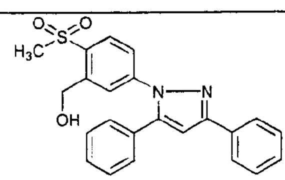
The following compounds are prepared by the procedure as described for example 1:

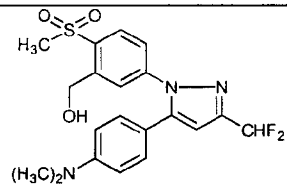
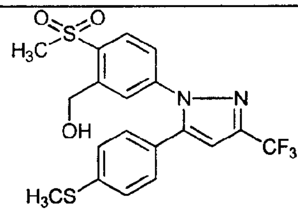
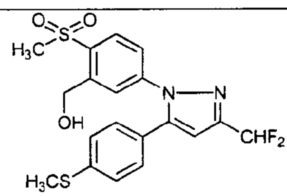
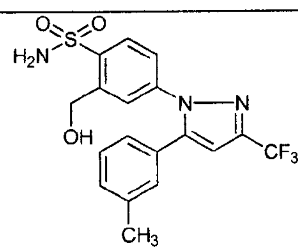
S. No.	Structure	Melting point	[1]HNMR
2		140 °C	($CDCl_3$, 200 MHz) δ : 7.95 (d, J = 8.49 Hz, 1H), 7.62 – 7.61 (m, 2H), 7.42 – 7.36 (m, 2H), 7.27 – 7.18 (m, 3H), 6.79 (s, 1H), 5.53 (bs, D_2O exchangeable, 2H), 5.00 (d, J = 4.65 Hz, 2H), 2.92 (bs, D_2O exchangeable, 1H).
3		132 °C	($CDCl_3$, 200 MHz) δ : 7.42 (s, 1H), 7.30 – 7.20 (m, 3H), 7.10 –7.05 (m, 3H), 6.28 (s, 1H), 4.66 (s, 2H), 2.36 (s, 3H), 2.33 (s, 3H).
4		188–189 °C	($CDCl_3$, 200 MHz) δ : 7.97 (d, J = 8.63 Hz, 1H), 7.62 (d, J = 1.89 Hz, 1H), 7.21 – 7.12 (m, 3H), 6.88 (d, J = 8.72 Hz, 2H), 6.71 (s, 1H), 5.43 (m, D_2O exchangeable, 2H), 5.01 (m, 2H), 3.83 (s, 3H), 2.65 (bs, D_2O exchangeable, 1H).
5		178–180 °C	($CDCl_3$, 200 MHz) δ : 8.00 (d, J = 8.40 Hz, 1H), 7.65 (d, J = 1.60 Hz, 1H), 7.30 – 7.15 (m, 3H), 7.10 (d, J = 8.20 Hz, 2H), 6.74 (s, 1H), 5.44 (bs, D_2O exchangeable, 2H), 5.04 (d, J = 3.80 Hz, 2H), 2.70 (bs, D_2O exchangeable, 1H), 2.50 (s, 3H).

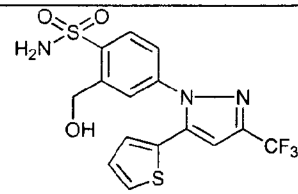
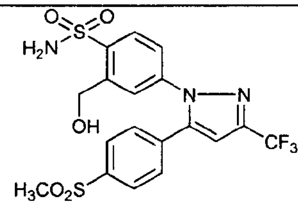
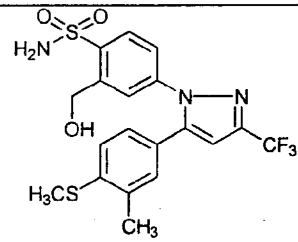
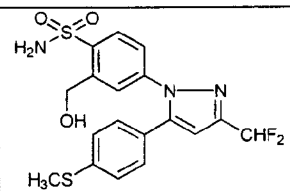
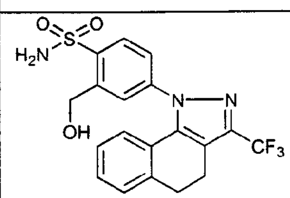
6		78 – 80 °C	($CDCl_3$, 200 MHz) δ : 7.92 (d, J = 8.80 Hz, 1H), 7.57 (d, J = 1.80 Hz, 1H), 7.44 (t, J = 7.00 Hz, 1H), 7.40 – 7.20 (m, 2H), 7.04 (t, J = 7.60 Hz, 1H), 6.85 (d, J = 8.40 Hz, 1H), 6.74 (s, 1H), 5.44 (bs, D_2O exchangeable, 2H), 4.98 (s, 2H), 3.41 (s, 3H), 2.75 (bs, D_2O exchangeable, 1H).
7		178–180 °C	($CDCl_3$, 200 MHz) δ : 7.96 (d, J = 8.60 Hz, 1H), 7.65 (d, J = 2.00 Hz, 1H), 7.29 – 7.24 (m, 1H), 7.05 (d, J = 8.81 Hz, 2H), 6.65 – 6.61 (m, 3H), 5.43 (bs, D_2O exchangeable, 2H), 5.03 (s, 2H), 2.99 (s, 6H), 2.65 (bs, D_2O exchangeable, 1H).
8		96–98 °C	($CDCl_3$, 200 MHz) δ : 7.86 (d, J = 8.20 Hz, 1H), 7.60 (s, 1H), 7.20 – 7.00 (m, 4H), 6.65 (s, 1H), 5.45 (bs, D_2O exchangeable, 2H), 4.95 (s, 2H), 2.80 (bs, D_2O exchangeable, 1H), 2.35 (s, 3H), 2.00 (s, 3H).
9		128–131 °C	($CDCl_3$, 200 MHz) δ : 7.95 (d, J = 8.40 Hz, 1H), 7.65 (s, 1H), 7.50 – 7.40 (m, 1H), 7.30 – 7.05 (m, 4H), 6.85 (s, 1H), 5.04 (bs, D_2O exchangeable, 2H), 5.00 (s, 2H), 2.90 (bs, D_2O exchangeable, 1H).
10		129–132 °C	($CDCl_3$, 200 MHz) δ : 7.90 (d, J = 8.40 Hz, 1H), 7.60 (s, 1H), 7.45 – 7.20 (m, 4H), 7.15 (d, J = 7.20 Hz, 1H), 6.80 (s, 1H), 5.50 (bs, D_2O exchangeable, 2H),

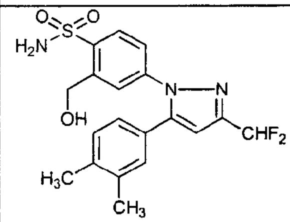
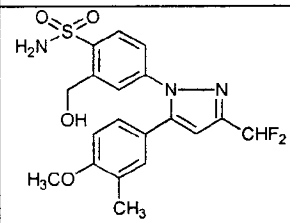
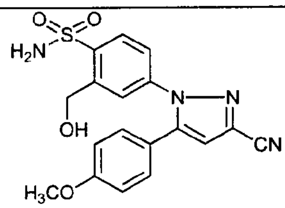
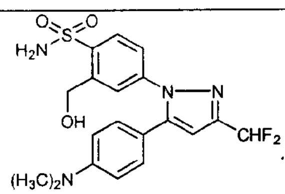
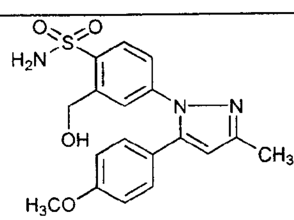
			4.95 (s, 2H), 2.80 (bs, D_2O exchangeable, 1H).
11		-	($CDCl_3$, 200 MHz) δ : 7.95 (d, J = 8.40 Hz, 1H), 7.59 (d, J = 2.00 Hz, 1H), 7.30 – 7.10 (m, 5H), 6.75 (s, 1H), 5.51 (bs, D_2O exchangeable, 2H), 4.98 (s, 2H), 2.88 (bs, D_2O exchangeable, 1H), 2.50 (d, J = 7.20 Hz, 2H), 2.00 – 1.75 (m, 1H), 0.90 (d, J = 6.80 Hz, 6H).
12		125–127 °C	($CDCl_3$, 200 MHz) δ : 8.02 (d, J = 8.40 Hz, 1H), 7.65 (s, 1H), 7.25 (s, 1H), 6.90 – 6.70 (m, 4H), 5.45 (bs, D_2O exchangeable, 2H), 5.05 (s, 2H), 3.92 (s, 3H), 3.80 (s, 3H), 2.65 (bs, D_2O exchangeable, 1H).
13		168 °C	($CDCl_3$, 200 MHz) δ : 7.98 (d, J = 8.60 Hz, 1H), 7.64 (d, J = 1.80 Hz, 1H), 7.30 – 7.10 (m, 5H), 6.74 (s, 1H), 5.43 (bs, D_2O exchangeable, 2H), 5.00 (s, 2H), 2.70 – 2.60 (m, 3H, 1H D_2O exchangeable), 1.25 (t, J = 7.80 Hz, 3H).
14		208 °C	($CDCl_3$ + DMSO, 200 MHz) δ : 7.98 (d, J = 8.39 Hz, 1H), 7.70 (s, 1H), 7.22 – 7.18 (m, 1H), 7.04 – 6.90 (m, 3H), 6.74 (s, 1H), 6.65 (s, D_2O exchangeable, 2H), 5.15 (t, D_2O exchangeable, 1H), 5.00 (d, 2H), 3.92 (s, 3H).

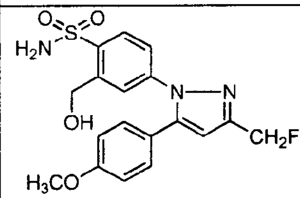
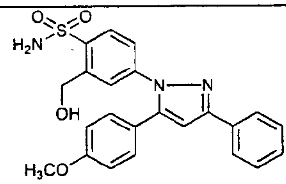
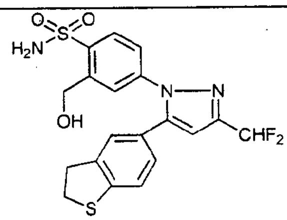
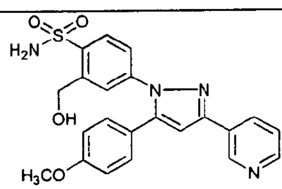
15		132–134 °C	($CDCl_3$, 200 MHz) δ : 7.95 (d, J = 8.40 Hz, 1H), 7.68 (s, 1H), 7.30 – 7.10 (m, 3H), 6.89 (d, J = 7.40 Hz, 1H), 6.74 (s, 1H), 5.50 (bs, D_2O exchangeable, 2H), 5.04 (s, 2H), 2.80 (bs, D_2O exchangeable, 1H), 2.32 (s, 3H), 2.29 (s, 3H).
16		180–182 °C	($CDCl_3$, 200 MHz) δ : 7.99 (d, J = 8.00 Hz, 1H), 7.64 (d, J = 1.80 Hz, 1H), 7.27 – 7.12 (m, 3H), 6.88 (d, J = 8.60 Hz, 2H), 6.72 (s, 1H), 5.43 (bs, D_2O exchangeable, 2H), 5.04 (s, 2H), 4.06 (q, J = 7.00 Hz, 2H), 2.65 (bs, D_2O exchangeable, 1H), 1.44 (t, J = 7.00 Hz, 3H).
17		130–132 °C	($CDCl_3$, 200 MHz) δ : 8.00 (d, J = 8.40 Hz, 1H), 7.65 (d, J = 2.00 Hz, 1H), 7.30 – 7.20 (m, 3H), 7.12 (d, J = 8.40 Hz, 2H), 6.78 (s, 1H), 5.45 (bs, D_2O exchangeable, 2H), 5.04 (d, J = 4.60 Hz, 2H), 3.00 (q, J = 7.40 Hz, 2H), 2.70 (bs, D_2O exchangeable, 1H), 1.39 (t, J = 7.20 Hz, 3H).
18		118–120 °C	($CDCl_3$, 200 MHz) δ : 7.99 (d, J = 8.00 Hz, 1H), 7.62 (d, J = 2.00 Hz, 1H), 7.27 – 7.23 (m, 2H), 6.83 – 6.67 (m, 3H), 5.39 (s, D_2O exchangeable, 2H), 5.00 (s, 2H), 3.88 (s, 3H), 3.74 (s, 3H), 2.65 (s, D_2O exchangeable, 1H).

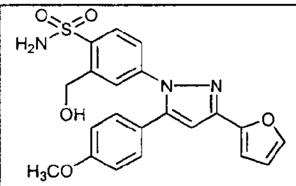
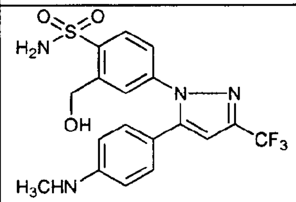
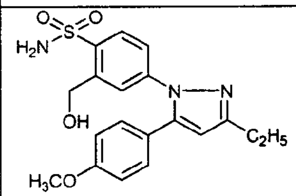
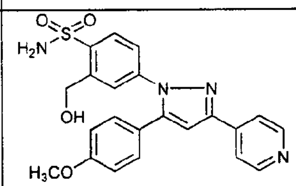
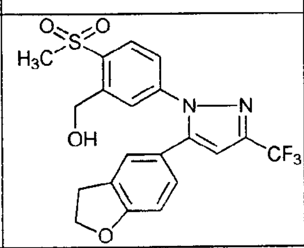
19		158–159 °C	($CDCl_3$, 200 MHz) δ : 8.00 (d, J = 8.40 Hz, 1H), 7.67 (d, J = 2.20 Hz, 1H), 7.40 – 7.20 (m, 2H), 7.07 (s, 1H), 6.94 (d, J = 7.80 Hz, 1H), 6.72 (s, 1H), 5.45 (bs, D_2O exchangeable, 2H), 5.04 (d, J = 4.80 Hz, 2H), 3.43 (t, J = 7.40 Hz, 2H), 3.30 (t, J = 7.60 Hz, 2H), 2.75 (bs, D_2O exchangeable, 1H).
20		172-174 °C	($CDCl_3$, 200 MHz) δ : 8.20 (d, J = 8.20 Hz, 1H), 7.81 – 7.67 (m, 4H), 7.11 (s, 1H), 6.96 (d, J = 8.80 Hz, 2H), 5.54 (bs, D_2O exchangeable, 2H), 5.13 (s, 2H), 3.87 (s, 3H).
21		166-167 °C	($CDCl_3$,+CD_3OD, 200 MHz) δ : 7.90 (d, J = 8.40 Hz, 1H), 7.73 (d, J = 2.00 Hz, 1H), 7.64 (d, J = 2.00 Hz, 1H), 7.15 – 7.05 (m, 3H), 6.88 (d, J = 8.80 Hz, 2H), 6.49 (d, J = 2.00 Hz, 1H), 4.96 (s, 2H), 3.82 (s, 3H).
22		66-71 °C	($CDCl_3$, 200 MHz) δ : 8.21 (d, J = 1.80 Hz, 1H), 7.80 (dd, J = 2.00 and 6.40 Hz, 1H), 7.20 – 7.00 (m, 3H), 6.95 – 6.70 (m, 4H), 4.58 (d, J = 6.80 Hz, 2H), 3.79 (s, 3H), 3.45 (t, D_2O exchangeable, 1H), 3.08 (s, 3H).
23		152-155 °C	($CDCl_3$, 200 MHz) δ : 8.18 (d, J = 2.00 Hz, 1H), 7.84 - 7.80 (m, 2H), 7.73 – 7.72 m, 1H), 7.69 – 7.19 (m, 8H), 7.02 (d, J = 8.40 Hz, 1H), 6.92 (s, 1H), 4.76 (bs, D_2O

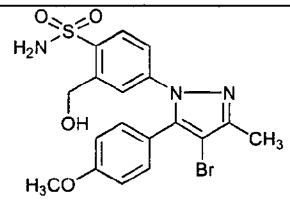
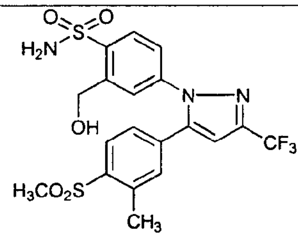
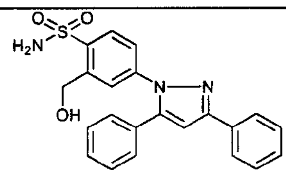
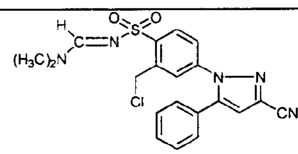
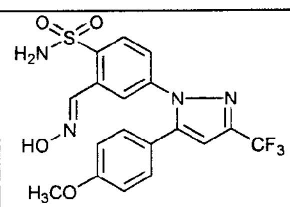
			exchangeable, 1H), 4.67 (s, 2H), 3.07 (s, 3H).
24		168-170°C	($CDCl_3$, 200 MHz) δ : 8.19 (s, 1H), 7.75 (d, J = 7.60 Hz, 1H), 7.19 (dd, J = 8.20 Hz, 1H), 7.00 – 6.94 (m, 3H), 6.69 (m, 1H), 6.59 (s, 1H), 6.55 (t, J = 54 Hz, 1H), 4.57 (d, J = 5.80 Hz, 2H), 3.60 (bs, D_2O exchangeable, 1H), 3.09 (s, 3H), 2.97 (s, 6H).
25		97-99 °C	($CDCl_3$, 200 MHz) δ : 8.27 (d, J = 1.80 Hz, 1H), 7.84 (dd, J = 1.80 and 7.40 Hz, 1H), 7.28 – 7.16 (m, 3H), 7.05 (d, J = 8.80 H, 2H), 6.85 (s, 1H), 4.60 (d, J = 7.00 Hz, 2H), 3.20 (t, D_2O exchangeable, 1H), 3.11 (s, 3H), 2.54 (s, 3H).
26		86-88 °C	($CDCl_3$, 200 MHz) δ : 8.24 (d, J = 1.80 Hz, 1H), 7.80 (dd, J = 2.40 and 5.80 Hz, 1H), 7.20 – 7.10 (m, 3H), 7.14 (d, J = 5.80 H, 2H), 6.82 (s, 1H), 6.76 (t, J = 54 Hz, 1H), 4.61 (d, J = 6.40 Hz, 2H), 3.47 (t, D_2O exchangeable, 1H), 3.11 (s, 3H), 2.49 (s, 3H).
27		131-134 °C	($CDCl_3$, 200 MHz) δ : 7.94 (d, J = 8.58 Hz, 1H), 7.63 (s, 1H), 7.25 – 7.23 (m, 3H), 6.96 – 6.95 (m, 2H), 6.75 (s, 1H), 5.41 (s, D_2O exchangeable, 2H), 5.02 (d, J = 4.24 Hz, 2H), 2.70 (t, D_2O exchangeable, 1H), 2.34 (s, 3H).

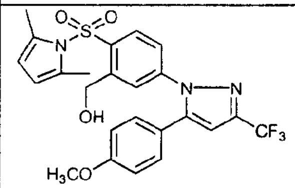
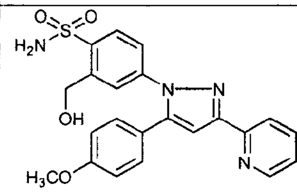
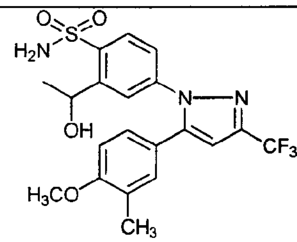
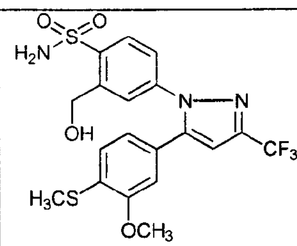
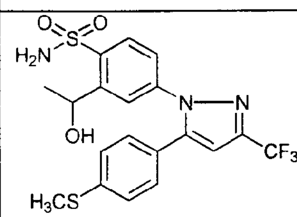
28		149-151 °C	($CDCl_3$, 200 MHz) δ : 8.06 (d, J = 8.20 Hz, 1H), 7.63 (s, 1H), 7.43 – 7.41 (m, 2H), 7.03 (t, J = 4.60 Hz, 1H), 6.92 (d, J = 3.60 Hz, 1H), 6.83 (s, 1H), 5.45 (bs, D_2O exchangeable, 2H), 5.05 (s, 2H), 2.69 (bs, D_2O exchangeable, 1H).
29		190-192 °C	(CD_3OD, 200 MHz) δ : 8.00 – 7.85 (m, 3H), 7.72 (s, 1H), 7.48 (d, J = 8.40 Hz, 2H), 7.25 (d, J = 6.60 Hz, 1H), 7.04 (s, 1H), 5.00 (s, 2H), 3.05 (s, 3H).
30		115-117 °C	($CDCl_3$, 200 MHz) δ : 8.00 (d, J = 8.80 Hz, 1H), 7.60 (s, 1H), 7.30 – 6.80 (m, 4H), 6.70 (s, 1H), 5.40 (bs, D_2O exchangeable, 2H), 5.00 (d, J = 4.40 Hz, 2H), 2.65 (bs, D_2O exchangeable, 1H), 2.47 (s, 3H), 2.28 (s, 3H).
31		166-167 °C	($CDCl_3$, 200 MHz) δ : 7.98 (d, J = 8.44 Hz, 1H), 7.61 (d, J = 1.98 Hz, 1H), 7.27 – 7.11 (m, 5H), 6.77 (t, J = 54.85 Hz, 1H), 6.73 (s, 1H), 5.48 (bs, D_2O exchangeable, 2H), 5.03 (d, J = 3.83 Hz, 2H), 2.80 (bs, D_2O exchangeable, 1H), 2.51 (s, 3H).
32		207-208 °C	($CDCl_3$, 200 MHz) δ : 8.17 (d, J = 8.40 Hz, 1H), 7.77 (d, J = 1.99 Hz, 1H), 7.63 – 7.58 (m, 1H), 7.38 – 7.26 (m, 2H), 7.09 (t, J = 7.80 Hz, 1H), 6.84 (d, J = 7.48 Hz, 1H), 5.55 (bs, D_2O exchangeable, 2H), 5.11 (d, J = 4.89 Hz, 2H), 3.08 – 3.01 (m,

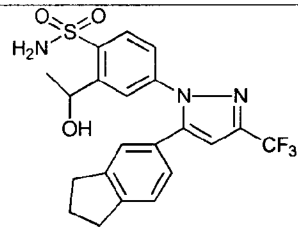
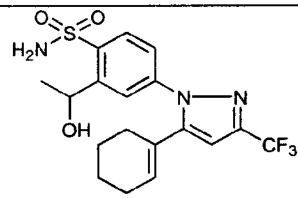
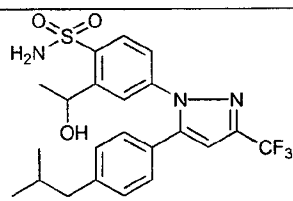
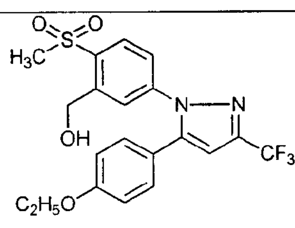
			2H), 2.92 – 2.85 (m, 2H).
33		140-142 °C	($CDCl_3$, 200 MHz) δ : 7.93 (d, J = 8.60 Hz, 1H), 7.60 (s, 1H), 7.26 – 7.06 (m, 4H), 6.87 (s, 1H), 6.69 (t, J = 54.0 Hz, 1H), 5.55 (s, D_2O exchangeable, 2H), 5.00 (s, 2H), 2.28 (s, 3H), 2.23 (s, 3H), 1.92 (bs, D_2O exchangeable, 1H).
34		164-166 °C	($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 7.95 (d, J = 8.40 Hz, 1H), 7.63 (s, 1H), 7.19 – 6.92 (m, 3H), 6.78 – 6.74 (m, 1H), 6.65 (s, 1H), 6.34 (t, J = 47.0 Hz, 1H), 4.95 (s, 2H), 3.84 (s, 3H), 2.38 (bs, D_2O exchangeable, 1H), 2.18 (s, 3H).
35		-	($CDCl_3$, 200 MHz) δ : 8.00 (d, J = 8.20 Hz, 1H), 7.61 (s, 1H), 7.25 – 7.14 (m, 1H), 7.12 (d, J = 8.80 Hz, 2H), 6.90 (d, J – 8.60 Hz, 2H), 6.82 (s, 1H), 5.42 (bs, D_2O exchangeable, 2H), 5.03 (s, 2H), 3.83 (s, 3H).
36		202-204 °C	(CD_3OD, 200 MHz) δ : 7.95 (d, J = 8.40 Hz, 1H), 7.85 (s, 1H), 7.25 (t, J = 6.60 Hz, 1H), 7.05 (d, J = 8.80 Hz, 2H), 6.80 – 6.65 (m, 3H), 6.64 (t, J = 52.0 Hz, 1H), 5.01 (s, 2H), 2.98 (s, 6H).
37		177-179 °C	($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 7.90 (d, J = 8.60 Hz, 1H), 7.62 (d, J = 1.80 Hz, 1H), 7.12 (d, J = 8.80 Hz, 2H), 7.10 (m, 1H), 6.85 (t, J = 8.80 Hz, 2H), 6.31 (s,

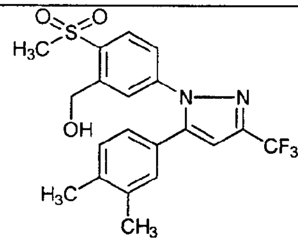
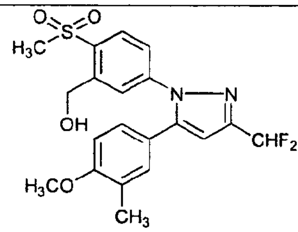
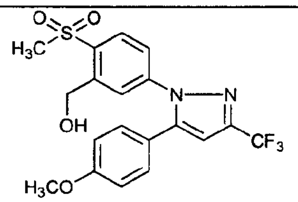
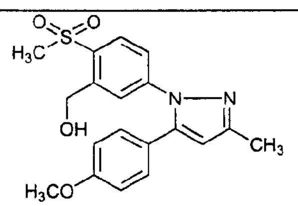
			1H), 4.96 (s, 2H), 3.82 (s, 3H), 2.38 (s, 3H).
38		148-150 °C	($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 7.87 (d, J = 8.40 Hz, 1H), 7.60 (d, J = 2.00 Hz, 1H), 7.36 (s, 1H), 7.12 (d, J = 8.80 Hz, 2H), 6.84 (d, J = 8.80 Hz, 2H), 6.54 (s, 1H), 6.53 (bs, D_2O exchangeable, 2H), 5.40 (d, J = 48.2 Hz, 2H), 4.90 (s, 2H), 3.80 (s, 3H), 2.90 (bs, D_2O exchangeable, 1H).
39		100-103 °C	($CDCl_3$, 200 MHz) δ : 8.00 – 7.80 (m, 3H), 7.65 – 7.62 (m, 1H), 7.60 – 7.20 (m, 6H), 7.03 – 6.85 (dd, J = 7.40 Hz, 55 : 45, 2H), 6.78 (ds, 55 : 45, 2H), 5.45 (bs, D_2O exchangeable, 2H), 5.00 (ds, 55 : 45), 3.86 (ds, 55 : 45).
40		160-162 °C	($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 7.90 (d, J = 8.40 Hz, 1H), 7.67 (d, J = 1.60 Hz, 1H), 7.20 – 7.00 (m, 3H), 6.85 (d, J = 7.00 Hz, 1H), 6.55 (s, 1H), 6.50 (t, J = 54.0 Hz, 1H), 4.99 (s, 2H), 3.47 – 3.20 (dt, J = 4.50 Hz, 4H).
41		190-192 °C	(CD_3OD, 200 MHz) δ : 9.08 (s, 1H), 8.51 (s, 1H), 8.35 (d, J = 8.00 Hz, 1H), 7.94 – 7.85 (m, 2H), 7.52 – 7.48 (m, 1H), 7.30 – 7.20 (m, 3H), 7.03 (s, 1H), 6.90 (d, J = 8.80 Hz, 2H), 4.99 (s, 2H), 3.78 (s, 3H).

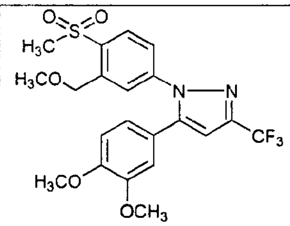
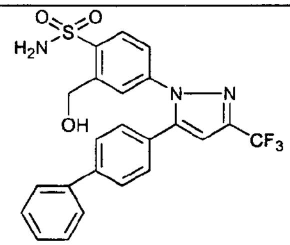
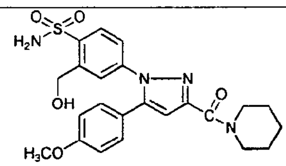
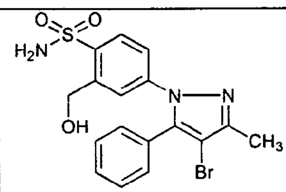
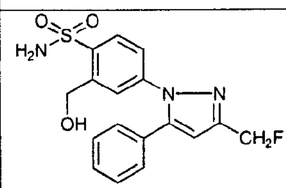
42		228-230 °C	(DMSO-d_6, 200 MHz) δ : 7.93 – 7.80 (m, 4H), 7.79 (s, 1H), 7.45 (d, J = 7.40 Hz, 1H), 7.25 (s, 1H), 7.05 – 7.00 (m, 2H), 6.65 (s, 1H), 6.45 (d, J = 3.20 Hz, 1H), 5.55 (bt, D_2O exchangeable, 1H), 4.94 (d, J = 4.60 Hz, 2H), 3.80 (s, 3H).
43		188-190 °C	(CD_3OD, 200 MHz) δ : 7.95 (d, J = 8.40 Hz, 1H), 7.83 (s, 1H), 7.30 (d, J = 6.40 Hz, 1H), 7.00 (d, J = 8.60 Hz, 2H), 6.75 (s, 1H), 6.54 (d, J = 8.40 Hz, 2H), 5.00 (s, 2H), 2.74 (s, 3H).
44		168-170 °C	($CDCl_3$, 200 MHz) δ : 7.75 (d, J = 8.80 Hz, 1H), 7.45 (d, J = 2.00 Hz, 1H), 7.06 (d, J = 8.80 Hz, 2H), 7.00 – 6.90 (m, 1H), 6.81 (d, J = 8.80 Hz, 2H), 6.27 (s, 1H), 5.88 (bs, D_2O exchangeable, 2H), 4.88 (s, 2H), 3.82 (s, 3H), 2.74 (q, J = 7.40 Hz, 2H), 1.30 (t, J = 7.40 Hz, 3H).
45		185-188 °C	(DMSO-d_6, 200 MHz) δ : 8.62 (d, J = 5.00 Hz, 2H), 8.00 – 7.80 (m, 3H), 7.49 (s, 1H), 7.28 – 7.20 (m, 4H), 6.95 (d, J = 8.40 Hz, 2H), 5.45 (bt, D_2O exchangeable, 1H), 4.87 (d, J = 4.40 Hz, 2H), 3.74 (s, 3H).
46		132-134 °C	($CDCl_3$, 200 MHz) δ : 8.23 (d, J = 2.00 Hz, 1H), 7.82 (dd, J = 2.00 and 8.20 Hz, 1H), 7.16 (d, J = 8.40 Hz, 1H), 6.96 (s, 1H), 6.88 (d, J = 8.20 Hz, 1H), 6.76 (m,

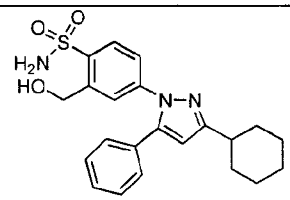
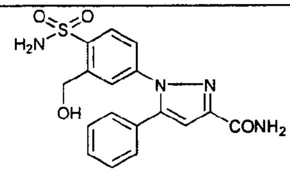
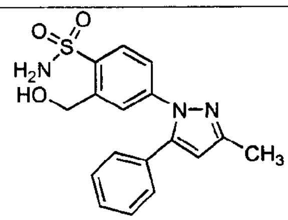
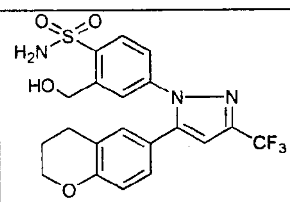
			2H), 4.63 (m, 4H), 3.34 (t, J = 6.80 Hz, D_2O exchangeable, 1H), 3.28 (t, J = 8.80 Hz, 2H), 3.08 (s, 3H).
47		100-102 °C	($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 7.85 (d, J = 8.62 Hz, 1H), 7.58 (d, J = 2.00 Hz, 1H), 7.20 (d, J = 8.80 Hz, 2H), 7.05 – 6.90 (m, 3H),4.96 (s, 2H), 3.84 (s, 3H), 2.38 (s, 3H).
48		174-176 °C	(DMSO-d_6, 200 MHz) δ : 7.86 – 7.82 (m, 2H), 7.59 (bs, D_2O exchangeable, 2H) 7.42 (s, 1H), 7.31 – 7.19 (m, 4H), 5.57 (bt, D_2O exchangeable, 1H), 4.91 (d, J = 3.80 Hz, 2H), 2.71 (s, 3H), 2.33 (s, 3H).
49		182-186 °C	($CDCl_3$, 200 MHz) δ : 7.94 – 7.88 (m, 2H), 7.62 (s 1H), 7.55 – 7.20 (m, 10H), 6.84 (s, 1H), 5.47 (bs, D_2O exchangeable, 2H) 4.98 (s, 2H), 3.00 (bs, D_2O exchangeable, 1H).
50		189-190 °C	($CDCl_3$, 200 MHz) δ : 8.05 (s, 1H), 7.95 (d, J = 8.60 Hz, 1H), 7.60 (s, 1H), 7.42 (m 2H), 7.30 – 7.17 (m, 3H), 6.85 (s, 1H), 5.06 (s, 2H), 3.12 (s, 3H), 3.04 (s, 3H).
51		216-218 °C	($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 11.00 (bs, D_2O exchangeable, 1H), 8.60 (s, 1H), 8.00 (d, J = 8.20 Hz, 1H), 7.92 (s, 1H), 7.26 (m, 1H), 7.15 (d, J = 8.60 Hz, 2H), 6.90 (d, J = 8.60 Hz, 2H), 6.70 (s, 1H), 6.25 (bs, D_2O exchangeable, 2H), 3.83 (s,

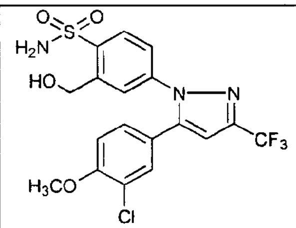
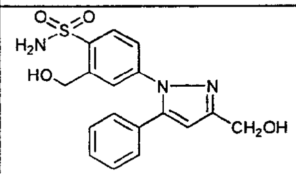
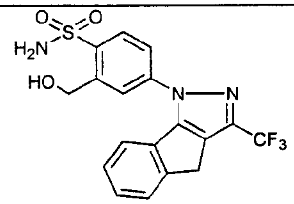
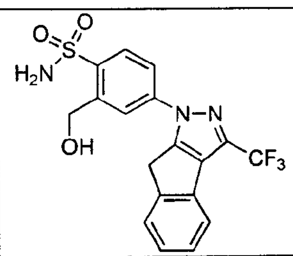
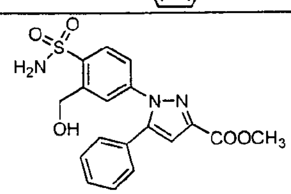
			3H).
52		130 °C	($CDCl_3$, 200 MHz) δ : 7.80 (s, 1H), 7.24 (d, J = 5.00 Hz, 1H), 7.20 (d, J = 11 Hz, 2H), 6.91 – 6.82 (m, 3H), 6.69 (s, 1H), 5.92 (s, 2H), 4.88 (s, 2H), 3.83 (s, 3H), 2.27 (s, 6H).
53		181-184 °C	(DMSO-d_6, 200 MHz) δ : 8.64 (d, J = 4.40 Hz, 1H), 8.10 – 7.80 (m, 4H), 7.52 (s, 1H), 7.40 (m, 1H), 7.15 – 7.05 (m, 3H), 6.96 (d, J = 8.40 Hz, 2H), 5.51 (bt, D_2O exchangeable, 1H), 4.90 (d, J = 4.40 Hz, 2H), 3.77 (s, 3H).
54		115 °C	(DMSO-d_6, 200 MHz) δ : 8.08 (d, J = 8.70 Hz, 1H), 7.68 (s, 1H), 7.48 (d, J = 6.50 Hz, 1H), 7.00– 6.90 (m, 2H), 6.80 (d, J = 8.40 Hz, 1H), 6.70 (s, 1H), 5.60 (q, J = 7.00 Hz, 1H), 5.35 (bs, D_2O exchangeable, 2H), 3.80 (s, 3H), 2.05(s, 3H), 1.58 (d, J = 6.50 Hz, 3H).
55		168-170 °C	(DMSO-d_6, 200 MHz) δ : 7.90 (d, J = 8.40 Hz, 1H), 7.73 (s, 1H), 7.20 (d, J = 6.60 Hz, 1H), 7.05 (d, J = 6.40 Hz, 1H), 6.85–6.75 (m, 2H), 6.73 (s, 1H), 4.90 (s, 2H), 3.75 (s, 3H), 3.25 (s, 3H).
56		90 °C	($CDCl_3$, 200 MHz) δ : 8.00 (d, J = 8.40 Hz, 1H), 7.55 (s, 1H), 7.35 (d, J = 8.50 Hz, 1H), 7.25– 7.10 (dd, J = 8.60 Hz, 4H), 6.75 (s, 1H), 5.68 (q, J = 6.20 Hz, 1H),

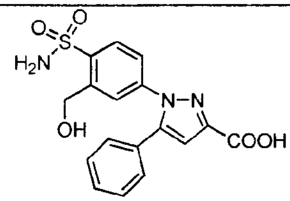
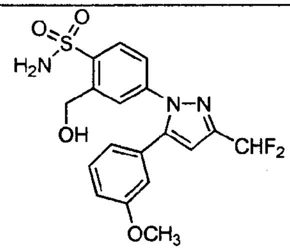
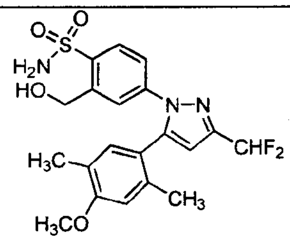
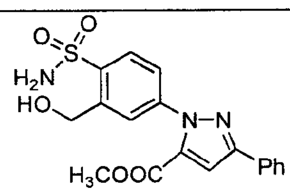
			5.40 (bs, D_2O exchangeable, 2H), 2.65 (bs, D_2O exchangeable, 1H), 2.50 (s, 3H), 1.45 (d, J = 5.80 Hz, 3H).
57		73.5 °C	($CDCl_3$, 200 MHz) δ : 8.05 (d, J = 8.50 Hz, 1H), 7.55 (s, 1H), 7.40 (d, J = 6.50 Hz, 1H), 7.30– 7.10 (m, 2H), 6.95 (d, J = 7.00 Hz, 1H), 6.70 (s, 1H), 5.68 (q, J = 5.50 Hz, 1H), 5.30 (bs, D_2O exchangeable, 2H), 2.90 (q, J = 7.40 Hz, 4H), 2.20 – 2.00 (m, 2H), 1.40 (d, J = 6.50 Hz, 3H).
58		145-146 °C	($CDCl_3$, 200 MHz) δ : 8.10 (d, J = 8.60 Hz, 1H), 7.80 (s, 1H), 7.60 (d, J = 6.50 Hz, 1H), 6.55 (s, 1H), 5.90 (s, 1H), 5.70 (q, J = 2.40 Hz, 1H), 5.30 (bs, D_2O exchangeable, 2H), 2.68 (bs, D_2O exchangeable, 1H), 2.10 (m, 4H), 1.60 (bm, 4H), 1.40 (d, J = 6.50 Hz, 3H).
59		-	($CDCl_3$, 200 MHz) δ : 8.05 (d, J = 5.00 Hz, 1H), 7.50 (m, 2H), 7.20 – 7.10 (bs, 4H), 6.80 (s, 1H), 5.60 (q, J = 4.50 Hz, 1H), 2.00 (d, J = 7.00 Hz, 2H), 1.95 – 1.75 (m, 1H), 1.40 (d, J = 8.00 Hz, 3H), 0.90 (d, J = 8.00 Hz, 6H).
60		146-148 °C	($CDCl_3$, 200 MHz) δ : 8.23 (d, J = 2.00 Hz, 1H), 7.80 (dd, J = 2.00 and 8.40 Hz, 1H), 7.18 – 7.02 (m, 3H), 6.84 (s, 1H), 6.79 (s, 2H), 4.58 (d, J = 6.20 Hz, 2H),

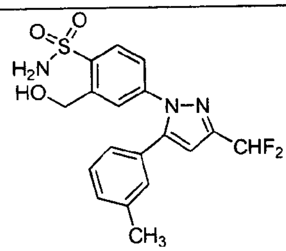
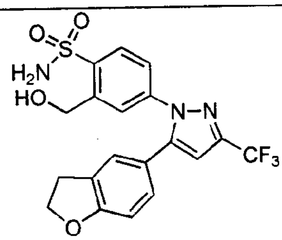
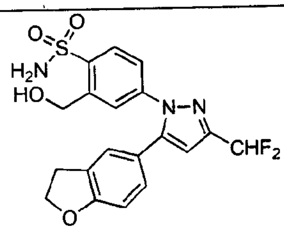
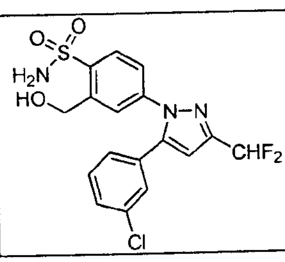
			4.02 (q, J = 7.20 Hz, 2H), 3.34 (bt, D_2O exchangeable, 1H), 3.09 (s, 3H), 1.41 (t, J = 6.80 Hz, 3H).
61		-	($CDCl_3$, 200 MHz) δ : 8.23 (d, J = 1.20 Hz, 1H), 7.78 (dd, J = 1.60 and 8.30 Hz, 1H), 7.18 (d, J = 8.40 Hz, 1H), 7.04 – 6.98 (m, 2H), 6.76 (m, 2H), 4.55 (s, 2H), 3.13 (s, 3H), 2.23 (s, 3H), 2.19 (s, 3H).
62		-	($CDCl_3$, 200 MHz) δ : 8.20 (s, 1H), 7.80 (dd, J = 1.80 and 8.30 Hz, 1H), 7.14 (d, J = 8.40 Hz, 1H), 7.00 (s, 1H), 6.76 – 6.66 (m, 4H), 4.56 (s, 2H), 3.81 (s, 3H), 3.08 (s, 3H), 2.14 (s, 3H).
63		136-140 °C	($CDCl_3$, 200 MHz) δ : 8.25 (d, J = 1.40 Hz, 1H), 7.84 (dd, J = 2.00 and 8.20 Hz, 1H), 7.19 (d, J = 8.20 Hz, 1H), 7.06 – 7.16 (d, J = 8.40 Hz, 2H), 6.90 – 6.80 (m, 3H), 4.60 (d, J = 5.80 Hz, 2H), 3.88 (s, 3H), 3.30 (bt, D_2O exchangeable, 1H), 3.17 (s, 3H).
64		162-164 °C	($CDCl_3$, 200 MHz) δ : 8.14 (d, J = 2.00 Hz, 1H), 7.72 (dd, J = 1.40 and 6.80 Hz, 1H), 7.06 – 6.98 (m, 3H), 6.80 (d, J = 8.80 Hz, 2H), 6.36 (s, 1H), 4.60 (s, 2H), 3.80 (s, 3H), 3.07 (s, 3H), 2.37 (s, 3H).

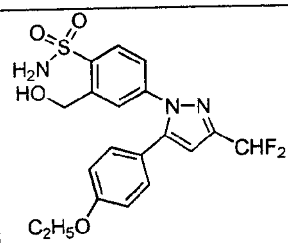
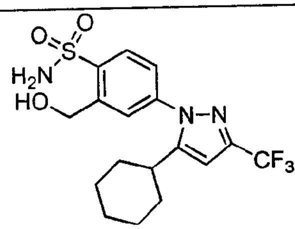
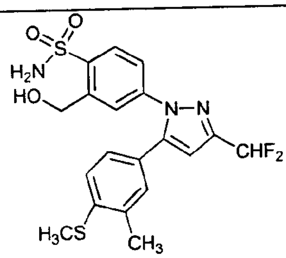
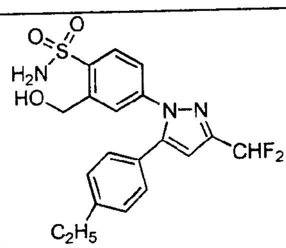
65		110 °C	($CDCl_3$, 200 MHz) δ : 8.20 (s, 1H), 7.85 (d, J = 6.50 Hz, 1H), 7.33 (d, J = 8.40 Hz, 1H), 7.00 (s, 1H), 6.85 – 6.65 (m, 3H), 4.30 (s, 2H), 3.80 (s, 3H), 3.30 (s, 3H), 3.00 (s, 3H), 2.10 (s, 3H).
66		182-184 °C	($CDCl_3$, 200 MHz) δ : 8.03 (d, J = 8.40 Hz, 1H), 7.68 – 7.60 (m, 5H), 7.51 – 7.33 (m, 3H), 7.28 – 7.26 (m, 3H), 6.83 (s, 1H), 5.45 (bs, D_2O exchangeable, 2H), 5.05 (d, J = 4.40 Hz, 2H), 2.73 (bs, D_2O exchangeable, 1H).
67		108-110 °C	($CDCl_3$, 200 MHz) δ : 7.90 (d, J = 8.60 Hz, 1H), 7.55 (s, 1H), 7.22 – 7.10 (m, 3H), 6.86 (d, J = 8.80 Hz, 2H), 6.71 (s, 1H), 5.56 (bs, D_2O exchangeable, 2H), 4.99 (s, 2H), 3.82 (s, 3H), 3.80 – 3.74 (m, 4H), 1.68 (m, 6H).
68		92-94 °C	($CDCl_3$, 200 MHz) δ : 7.78 (s, 1H), 7.68 (d, J = 8.40 Hz, 1H), 7.50 – 7.40 (m, 3H), 7.35 – 7.30 (m, 2H), 7.02 (d, J = 8.60 Hz, 1H), 5.45 (bt, D_2O exchangeable, 1H), 4.81 (d, J = 4.40 Hz, 2H), 2.30 (s, 3H).
69		105-110 °C	($CDCl_3$, 200 MHz) δ : 7.90 (d, J = 8.40 Hz, 1H), 7.55 (s, 1H), 7.45 – 7.30 (m, 2H), 7.30 - 7.15 (m, 4H), 6.64 (s, 1H), 5.50 (bs, D_2O exchangeable, 2H), 5.40 (d, J = 47 Hz, 2H), 4.98 (s, 2H).

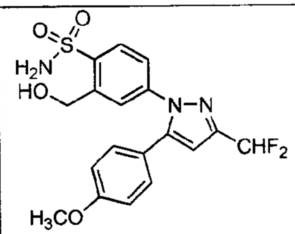
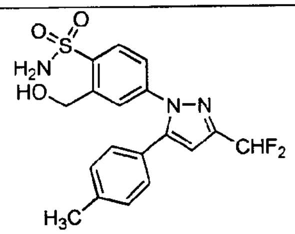
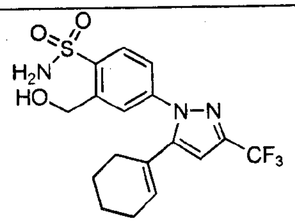
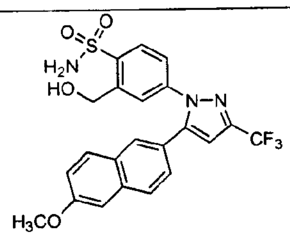
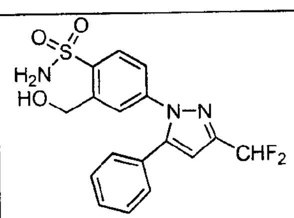
70		120-122 °C	($CDCl_3$, 200 MHz) δ : 8.16 (d, J = 8.40 Hz, 1H), 7.91 – 7.83 (m, 3H), 7.68 (s, 1H), 7.56 – 7.51 (m, 2H), 7.45 – 7.10 (m, 5H), [6.59 (s, 1H), 6.37 (s, 1H), : : 6 : 4], 5.70 – 5.40 (bd, D_2O exchangeable, 2H), 5.09 (s, 1H), 4.96 (s, 1H), 2.90 – 2.60 (m, 1H), 2.05 –1.20 (m, 10H).
71		240-241 °C	(DMSO-d_6, 200 MHz) δ : 7.95 – 7.85 (m, 1H), 7.80 – 7.75 (m, 1H), 7.55 (s, 1H), 7.43 – 7.40 (m, 2H), 7.40 – 7.25 (m, 3H), 7.04 (s, 1H), 6.70 (bs, D_2O exchangeable, 1H), 5.50 (bs, D_2O exchangeable, 2H), 4.90 (s, 2H).
72		118-124 °C	($CDCl_3$, 200 MHz) δ : 7.83 (d, J = 8.39 Hz, 1H), 7.50 (d, J = 1.66 Hz, 1H), 7.35 – 7.33 (m, 3H), 7.21 – 7.18 (m, 2H), 7.08 – 7.02 (m, 1H), 6.32 (s, 1H), 5.64 (s, D_2O exchangeable, 2H), 4.94 (s, 2H), 2.83 (s, 3H).
73		92-94 °C	($CDCl_3$, 200 MHz) δ : 7.98 (d, J = 8.60 Hz, 1H), 7.67 (d, J = 2.20 Hz, 1H), 7.26 (d, J = 8.20 Hz, 1H), 6.97 (s, 1H), 6.90 – 6.60 (m, 3H), 5.52 (bs, D_2O exchangeable, 2H), 5.04 (s, 2H), 4.25 (t, J = 5.00 Hz, 2H), 2.75 (t, J = 5.00 Hz, 2H), 2.06 – 1.97 (m, 2H).

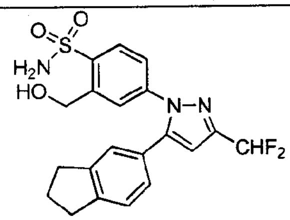
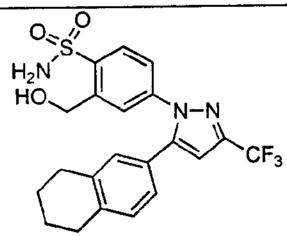
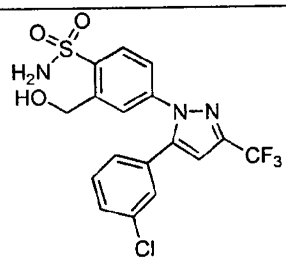
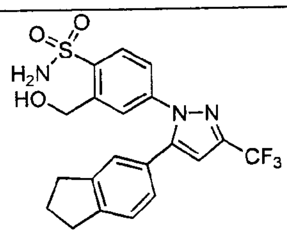
74		124-126 °C	($CDCl_3$, 200 MHz) δ : 7.94 (d, J = 8.40 Hz, 1H), 7.60 (s, 1H), 7.52 – 7.47 (m, 1H), 7.21 – 7.12 (m, 3H), 6.81 (s, 1H), 5.51 (bs, D_2O exchangeable, 2H), 4.98 (s, 2H), 3.55 (s, 3H), 3.03 (m D_2O exchangeable, 1H).
75		149-150 °C	($CDCl_3$, 200 MHz) δ : 7.82 (d, J = 7.60 Hz, 2H), 7.40 – 7.20 (m, 5H), 7.06 (d, J = 8.40 Hz, 1H), 6.51 (s, 1H), 5.28 (t, J = 5.00 Hz, D_2O exchangeable, 1H), 5.06 (t, J = 5.00 Hz, D_2O exchangeable, 1H), 4.95 (d, J = 4.60 Hz, 2H), 4.64 (d, J = 5.00 Hz, 2H).
76		203-204 °C	($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 8.25 (d, J = 8.40 Hz, 1H), 8.00 (s, 1H), 7.80 (d, J = 6.20 Hz, 1H), 7.55 (m, 2H), 7.35 (m, 2H), 6.45 (s, D_2O exchangeable, 2H), 5.10 (s, 2H), 3.75 (s, 2H).
77		172-174 °C	($CDCl_3$, 200 MHz) δ : 8.20 (d, J = 6.80 Hz, 1H), 7.80 – 7.60 (m, 2H), 7.58 – 7.50 (m, 1H), 7.40 – 7.30 (m, 3H), 5.15 (s, 2H), 3.90 (s, 2H).
78		169-170 °C	($CDCl_3$, 200 MHz) δ : 7.88 (d, J = 8.60 Hz, 1H), 7.63 (d, J = 2.00 Hz, 1H), 7.40 – 7.35 (m, 3H), 7.25 – 7.10 (m, 3H), 7.02 (s, 1H), 5.60 (bs, D_2O exchangeable, 2H), 4.98 (s, 2H), 3.97 (s, 3H), 2.05 (bs, D_2O exchangeable, 2H).

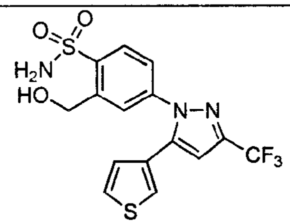
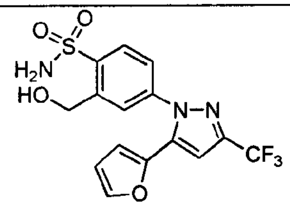
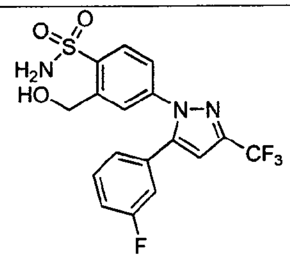
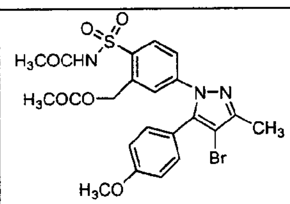
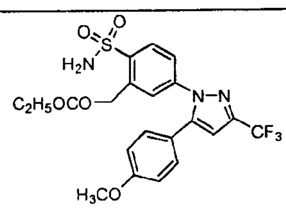
79		218-220 °C	($CDCl_3$, 200 MHz) δ : 7.85 (d, J = 8.40 Hz, 1H), 7.61 (s, 1H), 7.40 – 7.30 (m, 2H), 7.25 - 7.11 (m, 4H), 6.94 (s, 1H), 6.37 (bs, D_2O exchangeable, 2H), 4.86 (s, 2H), 2.75 (bs, D_2O exchangeable, 2H).
80		127 °C	($CDCl_3$, 200 MHz) δ : 7.94 (d, J = 8.30 Hz, 1H), 7.61 (s, 1H), 7.33 – 7.18 (m, 2H), 7.08 – 6.77 (m, 2H), 6.75 – 6.66 (m, 2H), 6.65 (t, J = 47.64 Hz, 1H), 5.61 (bs, D_2O exchangeable, 2H), 5.00 (d, J = 3.83 Hz, 2H), 3.78 (s, 3H), 3.12 (bs, D_2O exchangeable, 1H).
81		174 °C	($CDCl_3$, 200 MHz) δ : 7.86 (d, J = 8.63 Hz, 1H), 7.58 (d, J = 2.08 Hz, 1H), 7.13 – 6.99 (m, 3H), 6.63 (s, 1H), 6.59 (t, J = 47.5 Hz, 1H), 5.42 (bs, D_2O exchangeable, 2H), 4.95 (d, J = 4.25 Hz, 2H), 3.84 (s, 3H), 2.75 (bt, D_2O exchangeable, 1H), 2.16 (s, 3H), 1.89 (s, 3H).
82		179-180 °C	($CDCl_3$, 200 MHz) δ : 8.17 (d, J = 8.20 Hz, 1H), 7.86 (d, J = 6.40 Hz, 2H), 7. 57 – 7.60 (m, 2H), 7.50 –7.35 (m, 4H), 5.45 (bs, D_2O exchangeable, 1H), 5.12 (s, 2H), 3.87 (s, 3H)

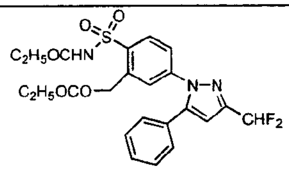
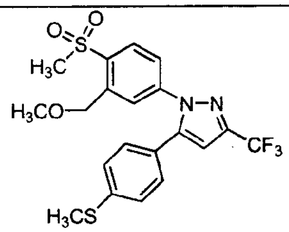
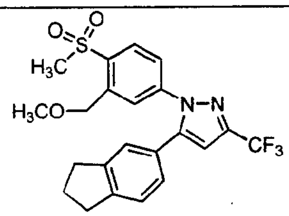
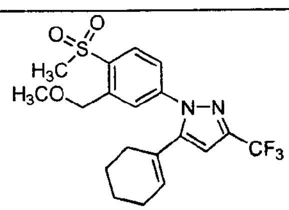
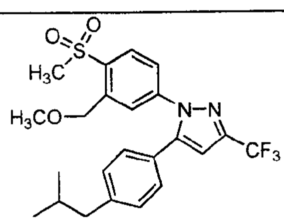
83		127 °C	($CDCl_3$, 200 MHz) δ : 7.96 (d, J = 8.54 Hz, 1H), 7.59 (s, 1H), 7.26 – 7.12 (m, 4H), 6.96 – 6.93 (m, 1H), 6.77 (t, J = 54.8 Hz, 1H), 6.76 (s, 1H), 5.44 (bs, D_2O exchangeable, 2H), 5.00 (d, J = 3.80 Hz, 2H), 2.75 (bt, D_2O exchangeable, 1H), 2.35 (s, 3H).
84		140-142 °C	($CDCl_3$, 200 MHz) δ : 8.02 (d, J = 8.20 Hz, 1H), 7.68 (d, J = 1.80 Hz, 1H), 7.26 (d, J = 7.00 Hz, 1H), 7.00 (m, 2H), 6.76 (d, J = 8.40 Hz, 1H), 6.71 (s, 1H), 5.46 (bs, D_2O exchangeable, 2H), 5.05 (s, 2H), 4.65 (t, J = 8.80 Hz, 2H), 3.22 (t, J = 9.60 Hz, 2H), 2.77 (bs, D_2O exchangeable, 1H).
85		76-78 °C	($CDCl_3$, 200 MHz) δ : 7.93 (d, J = 8.40 Hz, 1H), 7.59 (d, J = 1.60 Hz, 1H), 7.20 (d, J = 6.60 Hz, 1H), 7.05 (s, 1H), 6.92 (d, J = 8.00 Hz, 1H), 6.71 (d, J = 6.60 Hz, 1H), 6.66 (t, J = 54 Hz, 1H), 6.47 (s, 1H), 5.53 (bs, D_2O exchangeable, 2H), 4.99 (s, 2H), 4.61 (t, J = 8.80 Hz, 2H), 3.18 (t, J = 8.80 Hz, 2H), 3.05 (bs, D_2O exchangeable, 1H).
86		146-149 °C	($CDCl_3$, 200 MHz) δ : 8.00 (d, J = 8.30 Hz, 1H), 7.59 (d, J = 2.08 Hz, 1H), 7.40 – 7.10 (m, 4H), 7.09 (m, 1H), 6.79 (s, 1H), 6.78 (t, J = 54.93 Hz, 1H), 5.40 (s, D_2O

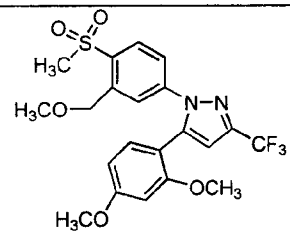
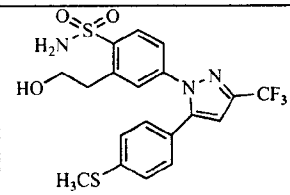
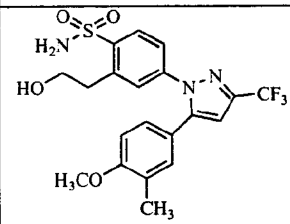
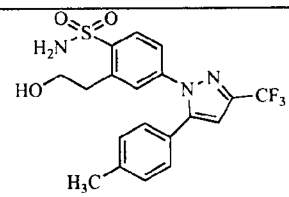
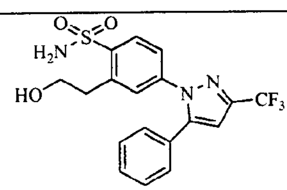
			exchangeable, 2H), 5.03 (s, 2H), 2.65 (bs, D_2O exchangeable, 1H).
87		150-152 °C	($CDCl_3$, 200 MHz) δ : 7.97 (d, J = 8.50 Hz, 1H), 7.58 (d, J = 2.00 Hz, 1H), 7.24 – 7.10 (m, 4H), 6.89 – 6.68 (m, 2H), 6.66 (t, J = 54.00 Hz, 1H), 5.45 (bs, D_2O exchangeable, 2H), 5.00 (s, 2H), 4.03 (q, J = 7.00 Hz, 2H), 2.78 (bs, D_2O exchangeable, 1H), 1.42 (t, J = 7.00 Hz, 3H).
88		-	($CDCl_3$, 200 MHz) δ : 8.15 (d, J = 8.50 Hz, 1H), 7.60 (s, 1H), 7.45 (d, J = 8.30 Hz, 1H), 6.50 (s, 1H), 5.50 (bs, D_2O exchangeable, 1H), 5.05 (s, 2H), 2.60 (m, 1H), 2.00 – 1.50 (m, 4H). 1.50 – 1.25 (m, 6H).
89		170-172 °C	($CDCl_3$, 200 MHz) δ : 7.96 (d, J = 8.60 Hz, 1H), 7.64 (d, J = 1.80 Hz, 1H), 7.25 (d, J = 8.00 Hz, 1H), 7.08 (d, J = 8.60 Hz, 2H), 6.96 (d, J = 6.60, 1H), 6.72 (t, J = 54.00 Hz, 1H), 6.66 (s, 1H), 5.50 (bs, D_2O exchangeable, 2H), 5.03 (s, 2H), 2.49 (s, 3H), 2.30 (s, 3H).
90		128-129 °C	($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 7.97 (d, J = 8.30 Hz, 1H), 7.60 (s, 1H), 7.28 – 7.12 (m, 5H), 6.79 (s, 1H), 6.77 (t, J = 48.50, 1H), 5.55 (s, D_2O exchangeable, 2H), 5.01 (s, 2H), 2.75 (q, J = 7.40 Hz,

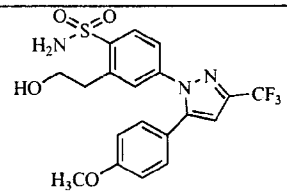
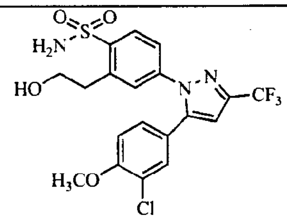
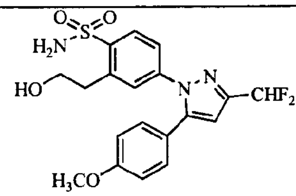
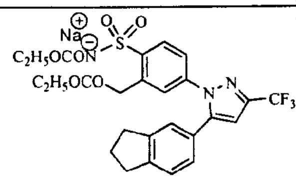
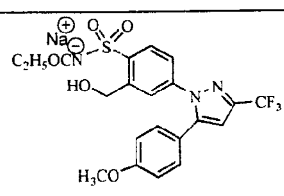
			2H), 1.89 – 1.79 (bs, D_2O exchangeable, 1H), 1.27 (t, J = 8.00 Hz, 3H).
91		166-168 °C	($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 7.94 (d, J = 6.00 Hz, 1H), 7.61 (s, 1H), 7.31 (s, 1H), 7.17 (d, J = 8.00 Hz, 2H), 6.90 (d, J = 7.00 Hz, 2H), 6.76 (t, J = 53.33 Hz, 1H), 6.67 (s, 1H), 6.28 (bs, D_2O exchangeable, 2H), 4.94 (s, 2H), 3.82 (s, 3H).
92		138 °C	($CDCl_3$, 200 MHz) δ : 7.95 (d, J = 8.35 Hz, 1H), 7.60 (d, J = 1.76 Hz, 1H), 7.26 – 7.09 (m, 5H), 6.77 (t, J = 54.85 Hz, 1H), 6.72 (s, 1H), 5.45 (s, D_2O exchangeable, 2H), 5.02 (d, J = 4.15 Hz, 2H), 2.75 (bs, D_2O exchangeable, 1H), 2.38 (s, 3H).
93		145-146 °C	($CDCl_3$, 200 MHz) δ : 8.15 (d, J = 9.00 Hz, 1H), 7.75 (s, 1H), 7.60 (d, J = 6.00 Hz, 1H), 6.55 (s, 1H), 5.95 (s, 1H), 5.50 (s, D_2O exchangeable, 2H), 5.10 (s, 2H), 2.20 – 1.50 (m, 8H).
94		207-208 °C	($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 7.90 (d, J = 8.45 Hz, 1H), 7.70 - 767 (m, 4H), 7.21 – 7.14 (m, 4H), 6.85 (s, 1H), 6.45 (s, D_2O exchangeable, 2H),4.96 (s, 2H), 3.94 (s, 3H).
95		131-132 °C	($CDCl_3$, 200 MHz) δ : 7.95 (d, J = 8.49 Hz, 1H), 7.57 (d, J = 1.99 Hz, 1H), 7.40 – 7.37 (m, 3H), 7.26 – 7.17 (m, 3H), 6.78 (t, J = 54.85 Hz, 1H), 6.75 (s, 1H), 5.47 (bs,

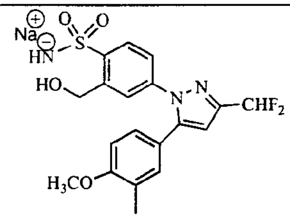
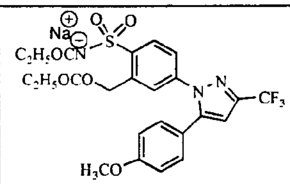
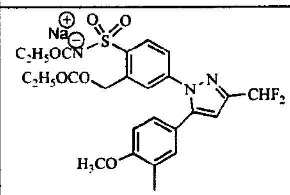
			D_2O exchangeable, 2H), 4.99 (s, 2H), 2.80 (bs, D_2O exchangeable, 1H).
96		99-100 °C	($CDCl_3$, 200 MHz) δ : 7.92 (d, J = 7.60 Hz, 1H), 7.63 (s, 1H), 7.05 – 7.30 (m, 3H), 6.92 (d, J = 7.40 Hz, 1H), 6.67 (t, J = 54 Hz, 1H), 6.50 (s, 1H), 5.50 (bs, D_2O exchangeable, 2H), 5.00 (s, 2H), 3.00 - 2.82 (m, 4H), 2.20 – 2.00 (m, 2H).
97		122-128 °C	($CDCl_3$, 200 MHz) δ : 7.96 (d, J = 8.53 Hz, 1H), 6.70 (d, J = 1.98 Hz, 1H), 7.24 – 7.19 (m, 1H), 7.04 – 7.00 (m, 2H), 6.86 – 6.82 (m, 1H), 6.72 (s, 1H), 5.44 (bs, D_2O exchangeable, 2H), 5.04 (s, 2H), 2.78 – 2.71 (m, 4H), 1.80 – 1.79 (m, 4H).
98		134-136 °C	($CDCl_3$, 200 MHz) δ : 8.00 (d, J = 8.53 Hz, 1H), 7.63 (m, 1H), 7.43 – 7.19 (m, 4H), 7.03 (d, J = 7.56 Hz, 1H), 6.80 (s, 1H), 5.47 (s, D_2O exchangeable, 2H), 5.03 (s, 2H), 2.80 (bs, D_2O exchangeable, 1H).
99		118-120 °C	($CDCl_3$, 200 MHz) δ : 8.00 (d, J = 8.40 Hz, 1H), 7.69 (s, 1H), 7.35 – 7.10 (m, 3H), 6.96 (d, J = 8.00 Hz, 1H), 6.74 (s, 1H), 5.40 (bs, D_2O exchangeable, 2H), 5.00 (s, 2H), 3.00 – 2.80 (m, 4H), 2.20 – 2.00 (m, 2H).

100		167 °C	($CDCl_3$ + DMSO-d_6, 200 MHz) δ : 8.00 (d, J = 8.30 Hz, 1H), 7.74 (s, 1H), 7.39 – 7.27 (m, 3H), 6.92 (d, J = 4.98 Hz, 1H), 6.81 (s, 2H D_2O exchangeable, 3H), 5.19 (m, D_2O exchangeable, 1H), 5.00 (d, J = 4.57 Hz, 2H).
101		158-160 °C	($CDCl_3$, 200 MHz) δ : 8.14 (d, J = 8.40 Hz, 1H), 7.63 (d, J = 1.80 Hz, 1H), 7.47 – 7.43 (m, 2H), 6.90 (s, 1H), 6.44 (d, J = 1.60 Hz, 1H), 6.32 (s, 1H), 5.49 (s, D_2O exchangeable, 2H), 5.07 (s, 2H), 2.75 (bs, D_2O exchangeable, 1H).
102		120-122 °C	($CDCl_3$, 200 MHz) δ : 8.02 (d, J = 8.40 Hz, 1H), 7.63 (s, 1H), 7.37 – 7.12 (m, 3H), 7.00 (d, J = 7.80 Hz, 2H), 6.79 (s, 1H), 5.41 (s, D_2O exchangeable, 2H), 5.03 (s, 2H), 2.65 (bt, D_2O exchangeable, 1H).
103		86-88 °C	($CDCl_3$, 200 MHz) δ : 9.05 (bs, D_2O exchangeable, 1H), 8.10 (d, J = 8.80 Hz, 1H), 7.52 (s, 1H), 7.40 – 7.20 (m, 3H), 6.95 (d, J = 8.80 Hz, 2H), 5.42 (s, 2H), 3.84 (s, 3H), 2.38 (s, 3H), 2.05 (s, 6H).
104		150-152 °C	(DMSO-d_6, 200 MHz) δ : 7.96 (d, J = 8.60 Hz, 1H), 7.73 (bs, D_2O exchangeable, 2H), 7.58 (d, J = 8.20 Hz, 1H), 7.42 (s, 1H), 7.26 (d, J = 8.40 Hz, 2H), 7.15 (s, 1H), 7.00 (d, J = 8.40 Hz, 2H), 5.43 (s, 2H), 3.77 (s, 3H), 2.24 (q, J = 7.60 Hz,

			2H), 1.00 (t, J = 7.40 Hz, 3H).
105		-	($CDCl_3$, 200 MHz) δ : 9.30 (bs, D_2O exchangeable, 1H), 8.14 (d, J = 8.60 Hz, 1H), 7.58 (s, 1H), 7.46 – 7.35 (m, 4H), 7.30 – 7.20 (m, 2H), 6.76 (t, J = 54.0 Hz, 1H), 6.74 (s, 1H), 5.47 (s, 2H), 2.30 (q, J = 7.60 Hz, 4H), 1.10 (t, J = 7.80 Hz, 6H).
106		120 °C	($CDCl_3$, 200 MHz) δ : 8.20 (s, 1H), 7.90 (d, J = 6.40 Hz, 1H), 7.35 – 7.20 (m, 1H), 7.10 (dd, J = 5.80 Hz, 4H), 6.88 (s, 1H), 4.30 (s, 2H), 3.30 (s, 3H), 3.08 (s, 3H), 2.50 (s, 3H).
107		98.3 °C	($CDCl_3$, 200 MHz) δ : 8.20 (s, 1H), 7.88 (d, J = 8.00 Hz, 1H), 7.35 (m, 1H), 7.20 – 7.10 (m, 2H), 6.80 (d, J = 7.80 Hz, 1H), 6.79 (s, 1H), 4.35 (s, 2H), 3.35 (s, 3H), 3.10 (s, 3H), 2.95 – 2.75 (m, 4H), 2.20 - 2.00 (m, 2H).
108		-	($CDCl_3$, 200 MHz) δ : 8.25 (s, 1H), 7.95 (d, J = 6.50 Hz, 1H), 7.45 (d, J = 8.30 Hz, 1H), 6.57 (s, 1H), 5.70 (s, 1H), 5.38 (s, 2H), 3.35 (s, 3H), 3.10 (s, 3H), 2.20 – 1.90 (m, 4H), 1.58 (m, 4H).
109		-	($CDCl_3$, 200 MHz) δ : 8.20 (s, 1H), 7.85 (d, J = 6.00 Hz, 1H), 7.30 (d, J = 8.20 Hz, 1H), 7.10 – 6.98 (m, 4H), 6.80 (s, 1H), 4.30 (s, 2H), 3.30 (s, 3H), 3.05 (s, 3H), 2.45 (d, J = 8.00 Hz, 2H), 1.90 – 1.80 (m,

			1H), 0.90 (d, J = 6.60 Hz, 6H).
110		-	($CDCl_3$, 200 MHz) δ : 8.25 (s, 1H), 7.90 (d, J = 6.60 Hz, 1H), 7.40 – 7.25 (m, 2H), 6.80 – 6.55 (m, 2H), 6.50 (s, 1H), 4.35 (s, 2H), 3.90 (s, 3H), 3.65 (s, 3H), 3.30 (s, 3H), 3.05 (s, 3H).
111		104-105 °C	($CDCl_3$, 200 MHz) δ : 8.06 (d, J = 8.60 Hz, 1H), 7.38 – 7.10 (m, 6H), 6.74 (s, 1H), 5.39 (bs, D_2O exchangeable, 2H), 3.92 (t, J = 5.40 Hz, 2H), 3.34 (t, J = 5.40 Hz, 2H), 2.49 (s, 3H).
112		99-100 °C	($CDCl_3$, 200 MHz) δ : 8.02 (d, J = 8.60 Hz, 1H), 7.40 (s, 1H), 7.39 – 6.74 (m, 4H), 6.69 (s, 1H), 5.70 (bs, D_2O exchangeable, 2H), 3.90 (t, J = 5.40 Hz, 2H), 3.84 (s, 3H), 3.32 (t, J = 5.40 Hz, 2H), 2.29 (s, 3H).
113		109-110 °C	($CDCl_3$, 200 MHz) δ : 8.02 (d, J = 8.80 Hz, 1H), 7.40 (s, 1H), 7.37 – 7.08 (m, 5H), 6.73 (s, 1H), 5.47 (bs, D_2O exchangeable, 2H), 3.90 (t, J = 5.40 Hz, 2H), 3.31 (t, J = 5.40 Hz, 2H), 2.37 (s, 3H).
114		101-102 °C	($CDCl_3$, 200 MHz) δ : 8.03 (d, J = 8.40 Hz, 1H), 7.40 – 7.25 (m, 7H), 6.77 (s, 1H), 5.48 (bs, D_2O exchangeable, 2H), 3.88 (t, J = 5.40 Hz, 2H), 3.32 (t, J = 5.40 Hz, 2H).

115		101-102 °C	($CDCl_3$, 200 MHz) δ : 8.06 (d, J = 8.40 Hz, 1H), 7.38 (s, 1H), 7.28 – 6.86 (m, 5H), 6.70 (s, 1H), 5.47 (bs, D_2O exchangeable, 2H), 4.05 (t, J = 5.40 Hz, 2H), 3.82 (s, 3H), 3.40 (t, J = 5.40 Hz, 2H).
116		49-50 °C	($CDCl_3$, 200 MHz) δ : 8.08 (d, J = 8.20 Hz, 1H), 7.39 – 7.01 (m, 5H), 6.75 (s, 1H), 5.48 (bs, D_2O exchangeable, 2H), 4.01 (t, J = 5.40 Hz, 2H), 3.94 (s, 3H), 3.39 (t, J = 5.40 Hz, 2H).
117		-	($CDCl_3$, 200 MHz) δ : 8.11 – 8.04 (m, 2H), 7.36 – 7.00 (m, 5H), 6.93 (s, 1H), 6.70 (s, 1H), 5.44 (bs, D_2O exchangeable, 2H), 4.07 (t, J = 5.60 Hz, 2H), 3.87 (s, 3H), 3.42 (t, J = 5.40 Hz, 2H).
118		146-148 °C	(DMSO-d_6, 200 MHz) δ : 7.86 – 7.82 (d, J = 8.20 Hz, 1H), 7.36 – 7.31 (d, J = 8.40 Hz, 1H), 7.24 – 7.20 (m, 3H), 7.11 (s, 1H), 6.99 – 6.96 (m, 1H), 5.46 (s, 2H), 2.84 – 2. 80 (m, 4H), 2.25 – 2.18 (m, 2H), 2.02 – 1.85 (m, 4H), 0.99 – 0.92 (t, J = 7.40 Hz, 3H), 0.87 – 0.79 (t, J = 7.80 Hz, 3H).
119		210-214 °C	(DMSO, 200 MHz) δ : 7.75 (d, J = 8.30 Hz, 1H), 7.61 (s, 1H), 7.25 (d, J = 8.80 Hz, 2H), 7.10 (s, 2H), 6.97 (d, J = 8.30 Hz, 2H), 5.24 (s, 1H), 4.87 (s, 2H), 3.76

			(s, 3H), 1.97 (q, J = 7.30 and 14.6 Hz, 2H), 0.84 (t, J = 7.80 Hz, 3H).
120		280-281 °C	($DMSO+CDCl_3$, 200 MHz) δ : 7.94 (d, J = 8.20 Hz, 1H), 7.46 (s, 1H), 7.09 – 6.93 (m, 3H), 6.77 – 6.73 (m, 2H), 6.61 (s, 1H), 4.87 (s, 2H), 3.82 (s, 3H), 3.34 (s, 1H), 2.16 (s, 3H).
121		210-212 °C	(CD_3OD, 200 MHz) δ : 8.15 (d, J = 8.30 Hz, 1H), 7.50 (d, J = 8.50 Hz, 1H), 7.37 (s, 1H), 7.26 (d, J = 8.50 Hz, 1H), 6.94 (t, J = 8.80 Hz, 3H), 5.64 (s, 2H), 3.85 (s, 3H), 3.36 (s, 1H), 2.35 – 2.15 (m, 4H), 1.15 – 1.03 (s, 6H).
122		198-201 °C	($CDCl_3$, 200 MHz) δ : 8.01 (d, J = 8.40 Hz, 1H), 7.43 (s, 1H), 7.05 – 6.89 (m, 3H), 6.73 – 6.64 (m, 3H), 5.55 (s, 2H), 3.79 (s, 3H), 2.20 – 2.14 (m, 7H), 1.02 – 0.88 (m, 6H).

The compounds of the present invention are tested *in vitro* for their COX-1 and COX-2 inhibitory activity using literature assay methods. The efficacy of the compound *in vivo* have been tested in male Sprague-Dawley rats using rat carrageenan foot paw edema test (Proc. Soc. Exp. Biol. Med., 111, 544 (1962); Laboratory models for testing NSAIDS in non steroidal antiinflammatory drugs (J. Lombardino ed., 1985).

In Vitro biochemical assays:

1. Spectrophotometric assay of cox-1 and cox-2 :

Microsomal fraction of ram seminal vesicles used as a source of cox-1 enzyme (Hemler et al., 1976) and microsomes from sf-9 cells infected with baculo virus containing

human cox-2 c-DNA used as a source of cox-2 enzyme (Wanda et al., 1994). Enzyme activity was measured using a chromogenic assay based on oxidation of N, N, N', N' - tetramethyl -p- phenylenediamine (TMPD) during the reduction of PGG_2 to PGH_2 as per the procedure described by Copeland et al., 1994 with following modifications. The assay mixture (1000μl) contains 100 μM Tris pH 8.0, 3μM EDTA, 15μM hematin, 150 units enzyme and 8% DMSO. The mixture was pre-incubated at 25^0C for 15 minutes before initiation of enzyme reaction in presence of compound/ vehicle. The reaction was initiated by the addition of 100μM arachidonic acid and 120μM TMPD. The enzyme activity is measured by estimation of the initial velocity of TMPD oxidation over the first 25 seconds of the reaction followed by increase in absorbency at 603 nM. The IC_{50} values were calculated using non-linear regression analysis of percent inhibitions.

S. No.	Example No.	COX-1 (100 μM)	COX-2 (100 μM)
1	1	264 ± 0.5	0.56 ± 0.03
2	15	108 ± 6	0.411 ± 0.04
3	19	64 ± 2	0.227 ± 0.005
4	27	327.3 ± 24	0.728 ± 0.076
5	30	130 ± 22.0	0.139 ± 0.024
6	31	41.2 ± 1.9	0.213 ± 0.022
7	36	39.5 ± 6.5	0.171 ± 0.018
8	47	0.0208.5 ± 6.5	0.48 ± 0.024
9	80	39.4 ± 7.3	0.236 ± 0.047
10	84	36.0 ± 16	0.228 ± 0.067
11	92	412 ± 9	0.502 ± 0.010
12	96	186 ± 18	0.562 ± 0.12

2) Human whole blood assay :

COX-1 inhibition assay

Fresh heparinised human whole blood was incubated with lipopolysaccharide (LPS) from *E. coli* at 100 μg/ml and with 2.5 μl vehicle (DMSO) or test compound for 24 hours at 37^0C. PGE_2 levels in the plasma were measured using EIA kit (Cayman chemicals, USA) after deproteinization.

COX-2 inhibition assay

An aliquot of fresh blood was mixed either with DMSO or test compounds and was allowed to clot for 1 hour at 37^0C. TXB_2 levels in the serum were measured using EIA kit (Cayman chemicals, USA) after deproteinization.

Example No.	COX-I IC_{50} (μM)	COX-II IC_{50} (μM)
4	5.38 ± 1.1	0.043 ± 0.007

***In vivo* screening methods :**

1. Carrageenan-induced rat paw edema:

Male Wistar rats (120-140 g) were fasted for 16 h before the experiment. Compounds were suspended in 0.25% CMC and administered orally in volume of 10 ml/kg 2 h before carrageenan injection. Hind paw edema induced in rats by intradermal injection of 50ul of 1% lambda-carrageenan in saline into the plantar surface of the right hind paw. Paw volume was measured before and 3 h after carrageenan injection by using plethysmometer (Ugo-Basile, Italy). Paw edema was compared with the vehicle control group and percent inhibition was calculated by taking the values in control group as 0%.

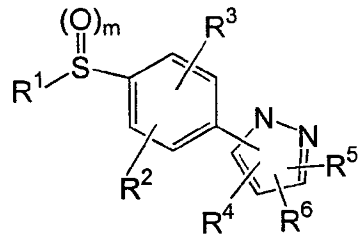
S. No.	Example No.	Dose	Percent inhibition
1	2	30	31
2	5	30	35
3	7	30	33
4	15	30	46
5	19	30	47
6	30	30	33
7	87	30	40
8	84	30	54

2. Carrageenan induced rat paw hyperalgesia:

Hyperalgesia to mechanical compression of the hind paw of male Wistar rats (150-170 g) was induced by intraplantar injection of carrageenan (2 mg per paw) 3 h before the study. Test compounds were given two hours after carrageenan injection. The vocalization response to compression of the carrageenan-injected paw was measured one hour later by analgesiometer (Ugo-Basile, Italy). For normal response one group was given intraplantar injection of saline. The percent hyperalgesia was calculated with difference in threshold in treated group versus control group compared to saline controls.

Claims :

1. A compound of formula (I)



(I)

its derivatives, its analogs, its tautomeric forms, its stereoisomers, its regioisomers, its polymorphs, its pharmaceutically acceptable salts, its pharmaceutically acceptable solvates, wherein R^1 represents amino or substituted or unsubstituted groups selected from alkyl, alkylamino, acylamino, cycloalkyl, cyclicamino, carboethoxycarbonylalkyl, hydrazino, hydrazido, aminoacid residue, aryl, heteroaryl or $-N=CR(NR)_2$ where R represents hydrogen or lower alkyl group; R^2 represents cyano, nitro, azido,. formyl, oximealkyl, thio or substituted or unsubstituted groups selected from amino, alkoxy, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacid residuealkyl, acyl, carbonyloxyalkyl, haloalkyl, aminoalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, thioalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, aralkoxyalkyl, carbonylalkyl, carboxamidoalkyl or carbonylaminoalkyl groups; R^3 represents hydrogen, halogen atom, hydroxy, nitro, cyano, azido or substituted or unsubstituted groups selected from hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, alkyl, alkoxy, hydroxyalkyl, alkoxyalkyl, acylamino or amino groups; R^4, R^5 and R^6 when attached to carbon atom may be same or different and independently represent hydrogen, halogen, hydroxy, cyano, nitro, thio, oxo, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, aralkoxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl,

aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, aromatic, single or fused, carbocycle or heterocycle ring; R^4, R^5 and R^6 when attached to nitrogen atom may be same or different and represent hydrogen, hydroxy, cyano, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, single or fused, aromatic, carbocycle or heterocycle groups; the pyrazole ring may be fused with R^4, R^5 or R^6 wherever possible and m is an integer in the range of 0-2.

2. A compound of formula (I) according to claim 1, wherein when the groups represented by R^1 are substituted, the substituents are selected from halogen, hydroxy, nitro, amino, cyano, alkyl, alkoxy, acyl, aryl, aralkyl or heteroaryl group.

3. A compound of formula (I) according to claim 1, wherein when the groups represented by R^2 are substituted, the substituents are selected from halogen, hydroxy, nitro, amino, thio, cyano, alkyl, haloalkyl, haloalkoxy, acyl, acyloxy, aryl, alkoxy, aralkyl, aralkoxy or carboxy group.

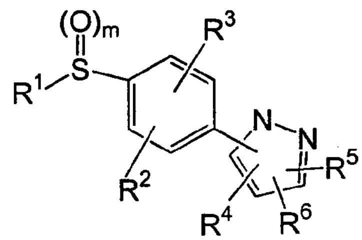
4. A compound of formula (I) according to claim 1, wherein when the groups represented by R^3 are substituted, the substituents are selected from nitro, halogen, amino, thio or cyano groups.

5. A compound of formula (I) according to claim 1, wherein when the groups represented by R^4, R^5 and R^6 are substituted, the substituents are selected from halogen, hydroxy, cyano, nitro, optionally halogenated $(C_1\text{-}C_6)$alkyl, optionally halogenated $(C_1\text{-}C_3)$alkoxy, acyl, amino, acylamino, cycloalkyl, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryloxy, heteroaralkyl, heteroaralkoxy,

heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heteroaryloxycarbonylamino, heteroaralkoxycarbonylamino, acyloxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, hydroxyalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, thio, thioalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, sulfonic acid or its derivatives or carboxylic or its derivatives, with a proviso that when the groups R^4, R^5 and R^6 represent phenyl, the phenyl group is not substituted by halogen or hydroxy in the 4^{th} position of the linkage with pyrazole.

6. A compound of formula (I) according to claim 1, wherein the ring structures formed by pyrazole fused with R^4, R^5 and R^6 are selected from benzothiopyranopyrazolyl, benzopyranopyrazolyl, benzindazolyl, naphthopyrazolyl, dihydrobenzindazolyl, dihydronapthopyrazolyl, dihydroindanopyrazolyl, benzopiperidinopyrazolyl, benzopiperidinopyrazolyl or pyranopyrazolyl.

7. A process for the preparation of compound of formula (I)

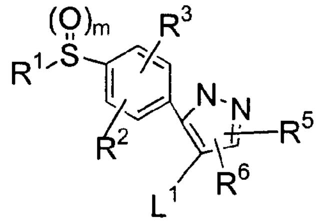


(I)

its derivatives, its analogs, its tautomeric forms, its stereoisomers, its regioisomers, its polymorphs, its pharmaceutically acceptable salts, its pharmaceutically acceptable solvates, wherein R^1 represents amino or substituted or unsubstituted groups selected from alkyl, alkylamino, acylamino, cycloalkyl, cyclicamino, carboethoxycarbonylalkyl, hydrazino, hydrazido, aminoacid residue, aryl, heteroaryl or $-N=CR(NR)_2$ where R represents hydrogen or lower alkyl group; R^2 represents cyano, nitro, azido, formyl, oximealkyl, thio or substituted or unsubstituted groups selected from amino, alkoxy, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacid residuealkyl, acyl, carbonyloxyalkyl, haloalkyl, aminoalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, thioalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl,

aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, aralkoxyalkyl, carbonylalkyl, carboxamidoalkyl or carbonylaminoalkyl groups; R^3 represents hydrogen, halogen atom, hydroxy, nitro, cyano, azido or substituted or unsubstituted groups selected from hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, alkyl, alkoxy, hydroxyalkyl, alkoxyalkyl, acylamino or amino groups; R^4, R^5 and R^6 when attached to carbon atom may be same or different and independently represent hydrogen, halogen, hydroxy, cyano, nitro, thio, oxo, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, aralkoxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, aromatic, single or fused, carbocycle or heterocycle ring; R^4, R^5 and R^6 when attached to nitrogen atom may be same or different and represent hydrogen, hydroxy, cyano, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, single or fused, aromatic, carbocycle or heterocycle groups and m is an integer in the range of 0-2., which comprises :

a) reacting a compound of formula (I-3)



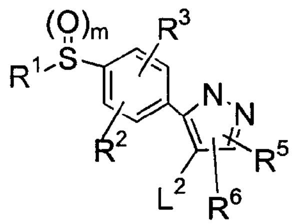
(I-3)

where L^1 represents $B(OR)_2$, wherein R represents hydrogen or lower alkyl group; R^1, R^2, R^3, R^5, R^6 and m are as defined above with a compound of formula (I-4)

$$R^4{-}L^2 \qquad \text{(I-4)}$$

where L^2 represents halogen atom or a leaving group and R^4 is as defined above ; or

b) reacting a compound of formula (I-7)



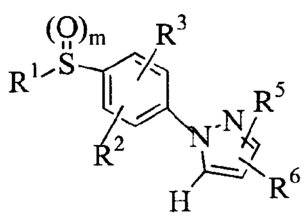
(I-7)

where L^2 represents halogen atom or a leaving group R^1, R^2, R^3, R^5, R^6 and m are as defined above with a compound of formula (I-8)

$$R^4{-}L^1 \qquad \text{(I-8)}$$

where L^1 represents $B(OR)_2$, wherein R represents hydrogen or lower alkyl group and R^4 is as defined above ; or

c) reacting a compound of formula (II-3)



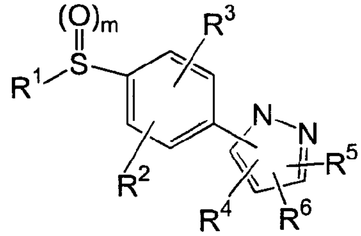
(II-3)

where R^1, R^2, R^3, R^5, R^6 and m are as defined above with a compound of formula (II-4)

$$R^4{-}L^3 \qquad \textbf{(II-4)}$$

where L^3 represents halogen atom and R^4 is as defined above; or

8. A process for the preparation of compound of formula (I)

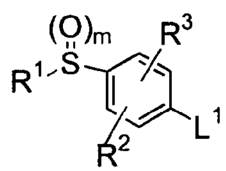


(I)

its derivatives, its analogs, its tautomeric forms, its stereoisomers, its regioisomers, its polymorphs, its pharmaceutically acceptable salts, its pharmaceutically acceptable solvates, wherein R^1 represents amino or substituted or unsubstituted groups selected from alkyl, alkylamino, acylamino, cycloalkyl, cyclicamino, carboethoxycarbonylalkyl, hydrazino, hydrazido, aminoacid residue, aryl, heteroaryl or –N=CR(NR)$_2$ where R represents hydrogen or lower alkyl group; R^2 represents cyano, nitro, azido, formyl, oximealkyl, thio or substituted or unsubstituted groups selected from amino, alkoxy, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacid residuealkyl, acyl, carbonyloxyalkyl, haloalkyl, aminoalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, thioalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, aralkoxyalkyl, carbonylalkyl, carboxamidoalkyl or carbonylaminoalkyl groups; R^3 represents hydrogen, halogen atom, hydroxy, nitro, cyano, azido or substituted or unsubstituted groups selected from hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, alkyl, alkoxy, hydroxyalkyl, alkoxyalkyl, acylamino or amino groups; R^4, R^5 and R^6 when attached to carbon atom may be same or different and independently represent hydrogen, halogen, hydroxy, cyano, nitro, thio, oxo, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, aralkoxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy,

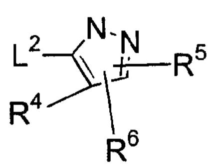
alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, aromatic, single or fused, carbocycle or heterocycle ring; R^4, R^5 and R^6 when attached to nitrogen atom may be same or different and represent hydrogen, hydroxy, cyano, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, single or fused, aromatic, carbocycle or heterocycle groups; the pyrazole ring may be fused with R^4, R^5 or R^6 wherever possible and m is an integer in the range of 0-2, which comprises :

a) reacting a compound of formula (I-1)



(I-1)

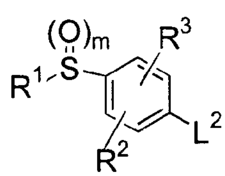
where L^1 represents $B(OR)_2$, wherein R represents hydrogen or lower alkyl group; R^1, R^2, R^3 and m are as defined above with a compound of (I-2)



(I-2)

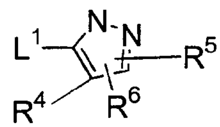
where L^2 represents halogen atom or a leaving group and R^4, R^5 and R^6 are as defined above ; or

b) reacting a compound of formula (I-5)



(I-5)

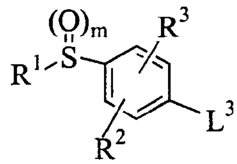
where L^2 represents halogen or leaving group; R^1, R^2, R^3 and m are as defined above with a compound of formula (I-6)



(I-6)

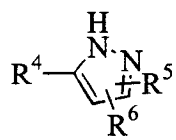
where L^1 represents $B(OR)_2$, wherein R represents hydrogen or lower alkyl group and R^4, R^5 and R^6 are as defined above ; or

c) reacting a compound of formula (II-1)



(II-1)

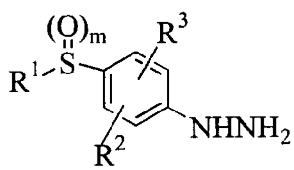
where L^3 represents halogen atom; R^1, R^2, R^3 and m are as defined above with a compound of formula (II-2)



(II-2)

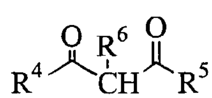
where R^4, R^5 and R^6 are as defined above ; or

d) reacting a compound of formula (III-1)



(III-1)

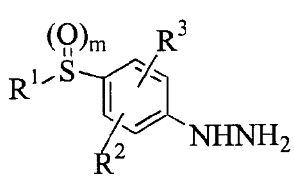
where R^1, R^2, R^3 and m are as defined above with a compound of formula (III-2)



(III-2)

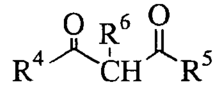
where R^4, R^5 and R^6 are as defined above; or

e) reacting a compound of formula (III-1)



(III-1)

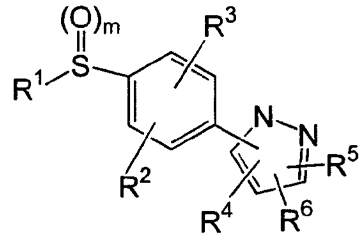
where R^1, R^2, R^3 and m are as defined above with a compound of formula (III-3)



(III-2)

where R^4, R^5 and R^6 are as defined above to produce a compound of formula (I).

9. A process for the preparation of compound of formula (I)

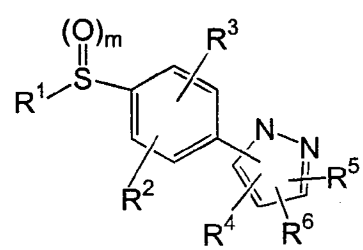


(I)

its derivatives, its analogs, its tautomeric forms, its stereoisomers, its regioisomers, its polymorphs, its pharmaceutically acceptable salts, its pharmaceutically acceptable solvates, wherein R^1 represents amino; R^2 represents cyano, nitro, azido, formyl, oximealkyl, thio or substituted or unsubstituted groups selected from amino, alkoxy, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacid residuealkyl, acyl, carbonyloxyalkyl, haloalkyl, aminoalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, thioalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, aralkoxyalkyl, carbonylalkyl, carboxamidoalkyl or carbonylaminoalkyl groups; R^3 represents hydrogen, halogen atom, hydroxy, nitro, cyano, azido or substituted or unsubstituted groups selected from hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, alkyl, alkoxy, hydroxyalkyl, alkoxyalkyl, acylamino or amino groups; R^4, R^5 and R^6 when attached to carbon atom may be same or different and independently represent hydrogen, halogen, hydroxy, cyano, nitro, thio, oxo, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, aralkoxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl,

aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, aromatic, single or fused, carbocycle or heterocycle ring; R^4, R^5 and R^6 when attached to nitrogen atom may be same or different and represent hydrogen, hydroxy, cyano, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated single or fused aromatic carbocycle or heterocycle groups; the pyrazole ring may be fused with R^4, R^5 or R^6 wherever possible and m is an integer in the range of 0-2, which comprises, transforming a compound of formula (I) where R^1 represents lower alkyl group, m represents 2 and all other symbols are as defined above in the presence of a Grignard reagent.

10. A process for the preparation of compound of formula (I)



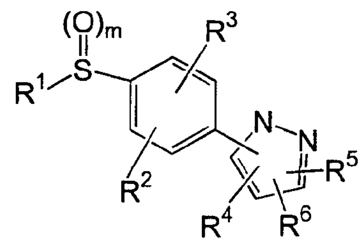
(I)

its derivatives, its analogs, its tautomeric forms, its stereoisomers, its regioisomers, its polymorphs, its pharmaceutically acceptable salts, its pharmaceutically acceptable solvates, wherein R^1 represents amino or substituted or unsubstituted groups selected from alkyl, alkylamino, acylamino, cycloalkyl, cyclicamino, carboethoxycarbonylalkyl, hydrazino, hydrazido, aminoacid residue, aryl, heteroaryl or –N=CR(NR)$_2$ where R represents hydrogen or lower alkyl group; R^2 represents cyano, nitro, azido, formyl, oximealkyl, thio or substituted or unsubstituted groups selected from amino, alkoxy,

hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacid residuealkyl, acyl, carbonyloxyalkyl, haloalkyl, aminoalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, thioalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, aralkoxyalkyl, carbonylalkyl, carboxamidoalkyl or carbonylaminoalkyl groups; R^3 represents hydrogen, halogen atom, hydroxy, nitro, cyano, azido or substituted or unsubstituted groups selected from hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, alkyl, alkoxy, hydroxyalkyl, alkoxyalkyl, acylamino or amino groups; R^4, R^5 and R^6 when attached to carbon atom may be same or different and independently represent hydrogen, halogen, hydroxy, cyano, nitro, thio, oxo, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, aralkoxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, aromatic, single or fused, carbocycle or heterocycle ring; R^4, R^5 and R^6 when attached to nitrogen atom may be same or different and represent hydrogen, hydroxy, cyano, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, single or fused, aromatic, carbocycle or heterocycle groups; the pyrazole ring may be fused with R^4, R^5 or R^6 wherever possible

and m is an integer of 1 or 2, which comprises, oxidising a compound of formula (I) where all symbols are as defined above and m represents 0 with an oxidising agent.

11. A process for the preparation of compound of formula (I)



(I)

its derivatives, its analogs, its tautomeric forms, its stereoisomers, its regioisomers, its polymorphs, its pharmaceutically acceptable salts, its pharmaceutically acceptable solvates, wherein R^1 represents amino or substituted or unsubstituted groups selected from alkyl, alkylamino, acylamino, cycloalkyl, cyclicamino, carboethoxycarbonylalkyl, hydrazino, hydrazido, aminoacid residue, aryl, heteroaryl or $-N{=}CR(NR)_2$ where R represents hydrogen or lower alkyl group; R^2 represents cyano, nitro, azido, formyl, oximealkyl, thio or substituted or unsubstituted groups selected from amino, alkoxy, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacid residuealkyl, acyl, carbonyloxyalkyl, haloalkyl, aminoalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, thioalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, aralkoxyalkyl, carbonylalkyl, carboxamidoalkyl or carbonylaminoalkyl groups; R^3 represents hydrogen, halogen atom, hydroxy, nitro, cyano, azido or substituted or unsubstituted groups selected from hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, alkyl, alkoxy, hydroxyalkyl, alkoxyalkyl, acylamino or amino groups; R^4, R^5 and R^6 when attached to carbon atom may be same or different and independently represent hydrogen, halogen, hydroxy, cyano, nitro, thio, oxo, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, aralkoxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl,

heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, aromatic, single or fused, carbocycle or heterocycle ring; R^4, R^5 and R^6 when attached to nitrogen atom may be same or different and represent hydrogen, hydroxy, cyano, hydroxylamino, substituted or unsubstituted groups selected from alkyl, alkoxy, acyl, acyloxy, amino, hydrazino, hydrazinoalkyl, hydrazido, hydrazidoalkyl, aminoacid residue, aminoacyl, carboxyalkyl, carboxyalkenyl, aryl, aryloxy, aralkyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heteroaryloxy, heteroaralkyl, heteroaralkoxy, heteroarylcarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, heterocyclylcarbonyl, aminocarbonyl, aminocarbonylalkyl, carbonylamino, cycloalkylacylamino, alkylaminoalkoxy, alkylaminoacyl, carboxylic acid or its derivatives, saturated or partially saturated, single or fused, aromatic, carbocycle or heterocycle groups; the pyrazole ring may be fused with R^4, R^5 or R^6 wherever possible and m is an integer of 0, which comprises, reducing a compound of formula (I) where all symbols are as defined above and m represents 1 or 2.

12. A compound as claimed in claim 1, which is selected from :

4-[5-(4-Methoxy-3-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide and its salts ;

4-[5-4-Phenyl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methylphenyl)-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methylsulfanylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(2-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Dimethylaminophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(2,4-Dimethylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(3-Fluorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(3-Chlorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Isobutylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(2,4-Dimethoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Ethylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(3-Fluoro-4-methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(3,4-Dimethylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Ethoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Ethylsulfanylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(3,4-Dimethoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(2,3-Dihydrobenzothien-5-yl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[3-(4-Methoxyphenyl)-5-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

5-[3-Difluoromethyl-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

5-[3,5-Diphenyl-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol ;

5-[3-Difluoromethyl-5-(4-dimethylaminophenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

5-[3-Trifluoromethyl-5-(4-methylsulfanylphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

5-[3-Difluoromethyl-5-(4-methylsulfanylphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

4-[5-(3-Methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-Thien-2-yl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methylsulfonylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methylsulfanyl-3-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methylsulfanylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

2-Hydroxymethyl-4-(3-trifluoromethyl-4,5-dihydro-1H-benzo[g]indazol-1-yl)-1-benzenesulfonamide and its salts ;

4-[5-(3,4-Dimethylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(3-Methyl-4-methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-3-cyano-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Dimethylaminophenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-methoxyphenyl)-3-fluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-3-phenyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(2,3-Dihydrobenzothien-5-yl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-3-(pyridin-3-yl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-3-(furan-2-yl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methylaminophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-3-ethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-3-(pyridin-4-yl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

5-[3-Trifluoromethyl-5-(2,3-dihydrobenzofuran-5-yl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

4-[5-(4-Methoxyphenyl)-4-bromo-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methylsulfonyl-3-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[3,5-Diphenyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide ;

N1-[(Z)-1-Dimethylaminomethylidene]-2-chloromethyl-4-[3-cyano-4-phenyl-1H-pyrazol-1-yl]-1-benzenesulfonamide and its salts ;

N1-[(E)-1-Dimethylaminomethylidene]-2-chloromethyl-4-[3-cyano-4-phenyl-1H-pyrazol-1-yl]-1-benzenesulfonamide and its salts ;

(Z) 2-Sulfamoyl-5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-benzaldehyde oxime and its salts ;

(E) 2-Sulfamoyl-5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-benzaldehyde oxime and its salts ;

2-(2,5-Dimethyl-1H-1-pyrrolylsulfonyl)-5-[5-(4-methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]phenyl methanol and its salts ;

4-[5-(4-Methoxyphenyl)-3-(pyridin-2-yl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxy-3-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide and its salts ;

4-[5-(4-Methylsulfanyl-3-methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methylsulfanylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide and its salts ;

4-[5-(2,3-Dihydro-1H-5-indenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide and its salts ;

4-[5-Cyclohexen-1-yl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide and its salts ;

4-[5-(4-Isobutylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide and its salts ;

5-[3-Trifluoromethyl-5-(4-ethoxyphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

5-[3-Trifluoromethyl-5-(3,4-dimethylphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

5-[3-Difluoromethyl-5-(4-methoxy-3-methylphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

5-[3-Trifluoromethyl-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

5-[3-Methyl-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

4-[5-(3,4-Dimethoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methoxymethyl phenyl sulfone and its salts ;

4-[5-[4-(Phenyl)phenyl]-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-3-piperidinocarbonyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-Phenyl-4-bromo-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-Phenyl-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-Phenyl-3-cyclohexyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

1-(3-Hydroxymethyl-4-sulfamoylphenyl)-5-phenyl-1H-3-pyrazole carboxamide and its salts ;

4-[5-Phenyl-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(2,3-Dihydrochroman-6-yl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(3-Chloro-4-methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-Phenyl-3-hydroxymethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

2-Hydroxymethyl-4-[3-trifluoromethyl-1,4-dihydroindeno[1,2-c]pyrazol-1-yl]-1-benzenesulfonamide and its salts ;

2-Hydroxymethyl-4-[3-trifluoromethyl-1,8-dihydroindeno[2,1-c]pyrazol-1-yl]-1-benzene sulfonamide and its salts ;

Methyl 1-(3-hydroxymethyl-4-sulfamoylphenyl)-5-phenyl-1H-3-pyrazol carboxylate and its salts ;

1-(3-Hydroxymethyl-4-sulfomoylphenyl)-5-phenyl-1H-3-pyrazole carboxylic acid and its salts ;

4-[5-(3-Methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxy-2,5-dimethylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

Methyl 1-(3-hydroxymethyl-4-sulfamoylphenyl)-3-phenyl-1H-5-pyrazole carboxylate and its salts ;

4-[5-(3-Methylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(2,3-Dihydrobenzofuran-5-yl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(2,3-Dihydrobenzofuran-5-yl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(3-Chlorophenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Ethoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-Cyclohexyl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methylsulfanyl-3-methylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Ethylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(4-Methylphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-Cyclohexen-1yl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(6-Methoxy-2-naphthyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-Phenyl-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(2,3-Dihydro-1H-5-indenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(1,2,3,4-Tetrahydro-6-naphthalenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(3-Chlorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(2,3-Dihydro-1H-5-indenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-Thien-3-yl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-Furan-2-yl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

4-[5-(3-Fluorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

2-Acetylsulfamoyl-5-[4-bromo-5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-1-yl]benzyl acetate and its salts ;

5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-sulfamoylbenzyl propanoate and its salts ;

2-Propanoylsulfamoyl-5-[5-phenyl-3-difluoromethyl-1H-pyrazol-1-yl]benzyl propanoate and its salts ;

1-(3-Methoxymethyl-4-methylsulfonylphenyl)-5-(4-methylsulfanylphenyl)-3-trifluoromethyl-1H-pyrazole and its salts ;

4-[5-(2,3-Dihydro-1H-inden-5-yl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methoxymethyl phenyl methyl sulfone and its salts ;

1-(3-Methoxymethyl-4-methylsulfonylphenyl)-5-cyclohexen-1-yl-3-trifluoromethyl-1H-pyrazole and its salts ;

4-[5-(4-Isobutylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methoxymethyl phenyl methyl sulfone and its salts ;

4-[5-(2,4-Dimethoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methoxymethyl phenyl methyl sulfone and its salts ;

4-[5-(4-Methylsulfanylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxy-3-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide and its salts ;

4-[5-(4-methylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide and its salts ;

4-[5-phenyl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(1-hydroxyethyl)-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxy-3-chlorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide and its salts ;

4-[5-(4-Methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide and its salts ;

4-[5-(4-Phenoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

5-[5-(4-Methoxyphenyl)-3-(2-pyridinyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

N-Propanoyl-2-hydroxymethyl-4-(3-trifluoromethyl-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]-1-benzenesulfonamide and its salts ;

4-[5-(3-Methyl-4-methoxyphenyl)-3-phenyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide and its salts ;

5-[5-(2,3-Dihydrobenzofuran-5-yl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

4-[5-(4-Isobutylphenyl)-3-phenyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide and its salts ;

4-[5-(4-Dimethylaminophenyl)-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide and its salts ;

4-[5-(3-Methyl-4-methoxyphenyl)-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide and its salts ;

1-(3-Hydroxymethyl-4-sulfamoylphenyl)-5-(4-methoxyphenyl)-1H-3-pyrazole carboxamide and its salts ;

4-[5-(3-Methyl-4-methoxyphenyl)-3-(2-pyridyl)-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide and its salts ;

5-[5-(6-Methoxy-2-naphthyl)-3-trifluoromethyl)-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

5-[5-(4-Methylsufanylphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-sulfamoyl benzyl propanoate and its salts ;

5-[5-(2,3-Dihydro-1H-5-indenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate and its salts ;

5-[5-(4-Phenoxyphenyl)-3-methyl-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

4-[5-(4-Phenoxyphenyl)-3-methyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzenesulfonamide and its salts ;

2-[1-(3-Hydroxymethyl-4-suflamoylphenyl)-5-(4-methoxyphenyl)-1H-3-pyrazolyl carboxamide]-1,3-thiazole and its salts ;

5-[5-(2,3-Dihydro-1H-5-indenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate and its salts ;

4-[5-(5-Indenyl)-3-methyl-1H-pyrazol-1-yl]-2-(2-hydroxyethyl)-1-benzenesulfonamide and its salts ;

5-[5-(2,3-Dihydro-1H-5-indenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-sulfamoyl benzyl propanoate and its salts ;

5-[5-(4-Phenoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methylsulfonyl phenyl methanol and its salts ;

5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methylsulfonyl benzaldehyde and its salts ;

5-[5-Phenyl-3-trifluoromethyl-1H-pyrazol-1-yl]-2-methylsulfonylphenyl methanol and its salts ;

5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate and its salts ;

5-[5-(3-Methyl-4-methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate and its salts ;

13. A compound according to claim 1 wherein the pharmaceutically acceptable salt is selected from Li, Na, K, Ca, Mg, Fe, Cu, Zn, Mn, N,N'-diacetylethylenediamine, betaine, caffeine, 2-diethylaminoethanol, 2-dimethylaminoethanol, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, hydrabamine, isopropylamine, methylglucamine, morpholine, piperazine, piperidine, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine, diethanolamine, meglumine, ethylenediamine, N,N'-diphenylethylenediamine, N,N'-dibenzylethylenediamine, N-benzyl phenylethylamine, choline, choline hydroxide, dicyclohexylamine, benzylamine, phenylethylamine, dialkylamine, trialkylamine, thiamine, aminopyrimidine, aminopyridine, purine, spermidine, alkylphenylamine, glycinol, phenyl glycinol, glycine, alanine, valine, leucine, isoleucine, norleucine,

tyrosine, cystine, cysteine, methionine, proline, hydroxy proline, histidine, ornithine, lysine, arginine, serine, threonine, phenylalanine, guanidine, substituted guanidine, ammonium, substituted ammonium or aluminum salts.

14. A compound according to claim 13, selected from

N-Propanoyl-2-hydroxymethyl-4-(3-trifluoromethyl-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]-1-benzenesulfonamide sodium salt ;

5-[5-(2,3-Dihydro-1H-5-indenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate sodium salt ;

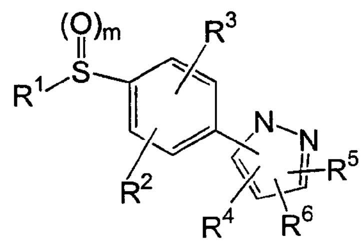
5-[5-phenyl-3-difluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate sodium salt ;

5-[5-(4-Methoxyphenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate sodium salt ;

5-[5-(3-Methyl-4-methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-propanoyl sulfamoyl benzyl propanoate;

4-[5-(3-Methyl-4-methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]-2-hydroxymethyl-1-benzene sulfonamide sodium salt ;

15. A pharmaceutical composition which comprises a compound of formula (I)



(I)

as defined in claim 1 or a compound as claimed in claim 12 and a pharmaceutically acceptable carrier, diluent, excipient or solvate.

16. A pharmaceutical composition as claimed in claim 15 in the form of a tablet, capsule, powder, syrup, solution or suspension.

17. A pharmaceutical composition which comprises a compound of formula (I) as defined in claim 1 or a compound as claimed in claim 12 and acetaminophen, phenacetin, caffeine, a H_2 antagonist, aluminum or magnesium hydroxide, simethicone,

phenylephrine, phenyl propanolamine, pseudophedrine, oxymetazoline, epinephrine, nephazoline, propylhexadrine or leavo-desoxyephedrine, xylomatazoline, a sedating or non sedating antihistamine, dextromethorphan, carbetapentane, caramiphen, hydrocodeine, codeine, a diuretic agent or their combination and a pharmaceutically acceptable carrier, diluent, excipient or solvate.

18. A method of treating inflammation, pyrexia, arthritis, pain, Alzheimer disease, dysmenorrhea, premature labor, asthma, bronchitis, inflammatory bowel disease, prostanoid-induced smooth muscle contraction, gastritis, irritable bowel syndrome, Crohn's disease, ulcerative colitis, diverticulitis, regional enteritis, peptic ulcers, cancer, bacterial infections, skin inflammation disorders such as eczema, burns, dermatitis, psoriasis, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, ophthalmic diseases such as retinitis, retinopathy, uveitis, ocular photophobia and acute injury to eye tissues, comprising administering a therapeutically effective amount of a compound of formula (I) as claimed in claim 1 or a compound as claimed in claim 12 or pharmaceutical composition as claimed in claim 15 to a mammal in need thereof.

19. A method according to claim 18, wherein the said pain is caused due to premature labor, back and neck pain, head ache, tooth ache, sprains, muscular pain, strains, myostis, neuralgia, synovitis, bursitis, tendinitis, injuries following surgical and dental procedures, pain from cancer, postoperative pain.

20. A method according to claim 18, wherein the inflammation is caused due to common cold, influenza, viral infections, pulmonary inflammation, post-operative inflammation, skin inflammation, inflammation in diseases such as vascular diseases, migraine head aches, periarteritis nodosa, thyroiditis, aplastic anemia, Behcat's syndrome, Hodgkin's diseases, scleroderma, myasthenia gravies, sarcoidosis, nephrotic syndrome, Type I diabetes, polymyositis, conjunctivitis, gingivitis, myocardial ischaemia, nephritis, swelling after injury, hypersensitivity.

21. A method according to claim 18, wherein the arthritis is selected from such as rheumatoid arthritis, osteoarthritis, gouty arthritis, juvenile arthritis, spondylo arthritis.

22. A method according to claim 18, for the treatment of inflammation, pyrexia, arthritis, pain, Alzheimer disease, dysmenorrhea, premature labor, asthma, bronchitis, inflammatory bowel disease, prostanoid-induced smooth muscle contraction, gastritis, irritable bowel syndrome, Crohn's disease, ulcerative colitis, diverticulitis, regional enteritis, peptic ulcers, cancer, bacterial infections, skin inflammation disorders such as eczema, burns, dermatitis, psoriasis, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, ophthalmic diseases such as retinitis, retinopathy, uveitis, ocular photophobia and acute injury to eye tissues, wherein the compound of formula (I) is a cyclooxygenase inhibitor.

23. A method according to claim 21, wherein the compound of formula (I) is preferably, a cyclooxygenase 2 inhibitor.

24. A method of treating inflammation, pyrexia, arthritis, pain, Alzheimer disease, dysmenorrhea, premature labor, asthma, bronchitis, inflammatory bowel disease, prostanoid-induced smooth muscle contraction, gastritis, irritable bowel syndrome, Crohn's disease, ulcerative colitis, diverticulitis, regional enteritis, peptic ulcers, cancer, bacterial infections, skin inflammation disorders such as eczema, burns, dermatitis, psoriasis, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, ophthalmic diseases such as retinitis, retinopathy, uveitis, ocular photophobia and acute injury to eye tissues, comprising administering a therapeutically effective amount of a pharmaceutical composition as claimed in claim 17 to a mammal in need thereof.

25. Use of a compound of formula (I) as defined in claim 1 or a compound as claimed in claim 12 or a pharmaceutical composition according to claim 15 for treating inflammation, pyrexia, arthritis, pain, Alzheimer disease, dysmenorrhea, premature labor, asthma, bronchitis, inflammatory bowel disease, prostanoid-induced smooth muscle contraction, gastritis, irritable bowel syndrome, Crohn's disease, ulcerative colitis, diverticulitis, regional enteritis, peptic ulcers, cancer, bacterial infections, skin inflammation disorders such as eczema, burns, dermatitis, psoriasis, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, ophthalmic

diseases such as retinitis, retinopathy, uveitis, ocular photophobia and acute injury to eye tissues.

26. Use of a compound according to claim 25, wherein the said pain is caused due to premature labor, back and neck pain, head ache, tooth ache, sprains, muscular pain, strains, myostis, neuralgia, synovitis, bursitis, tendinitis, injuries following surgical and dental procedures, pain from cancer, postoperative pain.

27. Use of a compound according to claim 25, wherein the inflammation is caused due to common cold, influenza, viral infections, pulmonary inflammation, post-operative inflammation, skin inflammation, inflammation in diseases such as vascular diseases, migraine head aches, periarteritis nodosa, thyroiditis, aplastic anemia, Behcat's syndrome, Hodgkin's diseases, scleroderma, myasthenia gravies, sarcoidosis, nephrotic syndrome, Type I diabetes, polymyositis, conjunctivitis, gingivitis, myocardial ischaemia, nephritis, swelling after injury, hypersensitivity.

28. Use of a compound according to claim 25, wherein the arthritis is selected from such as rheumatoid arthritis, osteoarthritis, gouty arthritis, juvenile arthritis, spondylo arthritis.

29. Use of a compound of formula (I) as defined in any one of claim 1 or a compound as claimed in claim 12 or a pharmaceutical composition as claimed in claim 15 for preparing a medicament for the treatment of inflammation, pyrexia, arthritis, pain, Alzheimer disease, dysmenorrhea, premature labor, asthma, bronchitis, inflammatory bowel disease, prostanoid-induced smooth muscle contraction, gastritis, irritable bowel syndrome, Crohn's disease, ulcerative colitis, diverticulitis, regional enteritis, peptic ulcers, cancer, bacterial infections, skin inflammation disorders such as eczema, burns, dermatitis, psoriasis, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, ophthalmic diseases such as retinitis, retinopathy, uveitis, ocular photophobia and acute injury to eye tissues, which comprising administering a therapeutically effective amount cyclooxygenase 2 inhibitor of formula (I) as claimed in claim 1.

30. Use of a compound according to claim 29, wherein the said pain is caused due to premature labor, back and neck pain, head ache, tooth ache, sprains, muscular pain, strains, myostis, neuralgia, synovitis, bursitis, tendinitis, injuries following surgical and dental procedures, pain from cancer, postoperative pain.

31. Use of a compound according to claim 29, wherein the inflammation is caused due to common cold, influenza, viral infections, pulmonary inflammation, post-operative inflammation, skin inflammation, inflammation in diseases such as vascular diseases, migraine head aches, periarteritis nodosa, thyroiditis, aplastic anemia, Behcat's syndrome, Hodgkin's diseases, scleroderma, myasthenia gravies, sarcoidosis, nephrotic syndrome, Type I diabetes, polymyositis, conjunctivitis, gingivitis, myocardial ischaemia, nephritis, swelling after injury, hypersensitivity.

32. Use of a compound according to claim 29, wherein the arthritis is selected from such as rheumatoid arthritis, osteoarthritis, gouty arthritis, juvenile arthritis, spondylo arthritis.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 00/00556

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D231/12 C07D409/04 C07D405/04 C07D401/04 C07D231/54
A61K31/415 A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 668 280 A (GEHRING REINHOLD ET AL) 26 May 1987 (1987-05-26) column 9, line 40 - line 45; claim 1	1-5
X	GB 1 389 550 A (HOECHST AG) 3 April 1975 (1975-04-03) examples 13,14	1,3-5
A	WO 95 15316 A (GRANETS MATTHEW J ;MIYASHIRO JULIE M (US); SEARLE & CO (US); TALLE) 8 June 1995 (1995-06-08) cited in the application claims; examples	1-5,15, 29
A	WO 98 22442 A (ANGELINI RICERCHE SPA ;PINZA MARIO (IT); TOMASELLI MAURO (IT); GIA) 28 May 1998 (1998-05-28) claims	1,15,29

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 August 2000	04/09/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	De Jong, B

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 99 64415 A (KATO TOMOKI ;PFIZER PHARMA (JP); ANDO KAZUO (JP); KAWAI AKIYOSHI () 16 December 1999 (1999-12-16) claims -----	1-5,15, 29

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-11,13,15-32 (all partially)

Present claims 1-11,13,15-32 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of these compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds of formula (I) in which the phenyl ring is attached to a nitrogen atom of the pyrazole ring and in which m=2.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/IB 00/00556

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4668280 A	26-05-1987	DE 3420985 A	25-04-1985
		AT 40120 T	15-02-1989
		AU 569916 B	25-02-1988
		AU 3410684 A	18-04-1985
		BR 8405151 A	27-08-1985
		CA 1233473 A	01-03-1988
		CA 1242207 A	20-09-1988
		DD 228157 A	09-10-1985
		DE 3476199 D	23-02-1989
		DK 491384 A	16-04-1985
		EP 0138149 A	24-04-1985
		ES 536768 D	16-07-1985
		ES 8506638 A	16-11-1985
		GR 80631 A	12-02-1985
		HU 36347 A	30-09-1985
		IL 73221 A	30-11-1988
		IL 83364 A	30-11-1988
		JP 60097948 A	31-05-1985
		KR 9007179 B	29-09-1990
		NZ 209874 A	05-12-1986
		TR 23212 A	21-06-1989
		US 4882437 A	21-11-1989
		US 4770693 A	13-09-1988
		US 4791212 A	13-12-1988
		ZA 8407986 A	26-06-1985
GB 1389550 A	03-04-1975	DE 2161553 A	20-06-1973
		BE 792587 A	12-06-1973
		CH 564064 A	15-07-1975
		FR 2162668 A	20-07-1973
		IN 138862 A	10-04-1976
		IT 971720 B	10-05-1974
		JP 852178 C	31-03-1977
		JP 48064276 A	06-09-1973
		JP 51025247 B	29-07-1976
WO 9515316 A	08-06-1995	US 5466823 A	14-11-1995
		US 5521207 A	28-05-1996
		AT 187965 T	15-01-2000
		AU 690609 B	30-04-1998
		AU 1171495 A	19-06-1995
		BR 1100406 A	08-02-2000
		CA 2177576 A	08-06-1995
		CN 1141630 A	29-01-1997
		CZ 9601503 A	11-12-1996
		DE 69422306 D	27-01-2000
		DE 69422306 T	18-05-2000
		EP 0731795 A	18-09-1996
		EP 0924201 A	23-06-1999
		EP 0922697 A	16-06-1999
		EP 0923933 A	23-06-1999
		ES 2141916 T	01-04-2000
		FI 962249 A	29-05-1996
		HU 74180 A	28-11-1996
		JP 2000109466 A	18-04-2000
		JP 3025017 B	27-03-2000
		JP 9506350 T	24-06-1997
		NO 962184 A	29-05-1996

Form PCT/ISA/210 (patent family annex) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/IB 00/00556

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9515316 A		NZ 276885 A	30-08-1999
		PL 314695 A	16-09-1996
		PT 731795 T	31-05-2000
		RU 2139281 C	10-10-1999
		US 5510496 A	23-04-1996
		US 5563165 A	08-10-1996
		US 5508426 A	16-04-1996
		US 5516907 A	14-05-1996
		US 5504215 A	02-04-1996
		US 5753688 A	19-05-1998
		US 5760068 A	02-06-1998
		ZA 9409418 A	28-11-1995
WO 9822442 A	28-05-1998	IT MI962385 A	15-05-1998
		AU 5552698 A	10-06-1998
WO 9964415 A	16-12-1999	AU 3841499 A	30-12-1999